Autoimmune Syndromes and Inflammatory Syndromes

Caused By Adjuvants In Vaccines

Also Known As

ASIA

A Two Smoking Guns Publication
Produced by Jeff Prager

Anarchy Books
Renegade Publishing

In the peer reviewed report, 'Novel Pebbles In The Mosaic Of Autoimmunity' the authors write,

"An entirely new syndrome, the autoimmune/inflammatory syndrome induced by adjuvants (ASIA), has been recently described. This is the new wind blowing within the branches of autoimmunity ..."

ALUMINUM

In
Vaccines

• The Independent Peer Reviewed Literature •

on
Autoimmune/Inflammatory Syndrome Induced By Adjuvants In Vaccines

ASIA

*safety levels for mercury and aluminum injected into the human body have never been medically determined...

Anarchy Books and Renegade Publications reminds you, we all might have to use their funny money. but don't drink their water, don't eat their food and don't buy their stuff!

Funded entirely by generous donations from our proud sponsors at Merck, Wyeth/Pfizer, GlaxoSmithKline, Sanofi, Novartis and the CDC

Libraries File As: A Runaway Slaves Horror Story

“Currently, ethylmercury (EtHg) and adjuvant-Al are the dominating interventional exposures encountered by fetuses, newborns, and infants due to immunization with Thimerosal-containing vaccines (TCVs). Despite their long use as active agents of medicines and fungicides, the safety levels of these substances have never been determined, either for animals or for adult humans—much less for fetuses, newborns, infants, and children”

From the International Journal of Environmental Research and Public Health
January 2015 by JG Dorea

Exposure to mercury and aluminum in early life:
developmental vulnerability as a modifying factor in neurologic and immunologic effects

Department of Nutrition, Faculty of Health Sciences,
Universidade de Brasilia, 70919-970 DF Brasilia, Brazil.
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http://www.ncbi.nlm.nih.gov/pubmed/25625408

"Aluminum is now being implicated as interfering with a variety of cellular and metabolic processes in the nervous system and in other tissue."

~ American Academy of Pediatrics

"Our results show that children from countries with the highest Autism Spectrum Disorder prevalence appear to have the highest exposure to aluminum from vaccines."

~ Journal of Inorganic Biochemistry

"Our results provide strong evidence supporting a link between autism and aluminum in vaccines..."

~ Entropy 2012

Aluminum (Al), the most commonly used vaccine adjuvant, is a demonstrated neurotoxin
and a strong immune stimulator. Hence, adjuvant Al has the potential to induce neuro-immune disorders."

~ Journal of Inorganic Biochemistry

"In adult humans Aluminum vaccine adjuvants have been linked to a variety of serious autoimmune and inflammatory conditions (i.e., ASIA), yet children are regularly exposed to much higher amounts of Al from vaccines than adults; it is often assumed that peripheral immune responses do not affect brain function. However, it is now clearly established that there is a bi-directional neuro-immune cross-talk that plays crucial roles in immunoregulation as well as brain function."

~ Lupus 2012

There Is An Unrecognized AUTOIMMUNE EPIDEMIC In The USA

More Americans suffer from Autoimmune Disorders than Cancer and Heart Disease

There is a silent epidemic of enormous proportions composed of Autoimmune Diseases—nearly 100 different illnesses—that have already affected millions of Americans. Autoimmune Disease is now a major American health problem. The National Institutes of Health estimate that there are 23.5 million Americans suffering from Autoimmune Disease and the American Autoimmune Related Diseases Association estimates that there are 50 million Americans suffering from one Autoimmune Disease or another.

The NIH includes data from 24 diseases for which good epidemiology studies are available and AARDA uses a wider estimate. Researchers have actually identified 80-100 different Autoimmune Diseases and suspect that another 40 illnesses have an autoimmune basis. These diseases are generally chronic and often deadly.

Autoimmune Disease is now one of the top ten leading causes of death in female children and women in all age groups up to 64 years of age and commonly used immunosuppressant treatments frequently lead to devastating long term side effects. An autoimmune disease diagnosis can be life-threatening.

There are critical factors creating obstacles in the diagnosis and treatment of Autoimmune Disease. Symptoms cross many medical specialties and can affect all body organs, the medical education system provides minimal learning about Autoimmune Disease, specialists are often unaware of interrelationships among the different autoimmune diseases or advances in treatment outside their own specialty area, initial symptoms are often intermittent and unspecific until the disease becomes acute and research is generally disease-specific and limited in scope.

Cancer affects 9 million Americans and heart disease affects 22 million Americans which means Autoimmune Disease affects more people in America than any other single illness. Yet research funding for cancer and heart disease ranges in the billions while Autoimmune Disease research funds languish in the low millions. Autoimmune Disease ranked #1 in a top ten list of most popular health topics requested by callers to the National Women's Health Information Center because Autoimmune Disease affects far more women than men.

Table Of Contents

Page 1 - Over 100 Peer Reviewed Reports & Studies and a few ditties about Macrophagic Myofasciitis (MMF), ASIA, Arthritis, Gulf War Syndrome (GWS), Apoptosis, Necrosis, Vaccines, the Normal Inflammatory Response and some other really important stuff.

January 2016
A Runaway Slaves Publication

* Guns, Ammo and Money are preferred 4 to 1 over Vaccines by 9 out of 10 Americans Surveyed

From the Romanian Journal of Internal Medicine • July 2013

ASIA or Shoenfeld's syndrome an autoimmune syndrome induced by adjuvants

Cojocaru M, Chico B.

Abstract

Recently, reports have suggested grouping different autoimmune conditions that are triggered by external stimuli as a single syndrome called autoimmune syndrome induced by adjuvants (ASIA). This syndrome is characterized by the appearance of myalgia, myositis, muscle weakness, arthralgia, arthritis, chronic fatigue, sleep disturbances, cognitive impairment and memory loss, and the possible emergence of a demyelinating autoimmune disease caused by systemic exposure after vaccines and adjuvants. As there are no markers for ASIA, the authors intend to present ASIA, or Shoenfeld's syndrome, as an autoimmune syndrome induced by adjuvants.

http://www.ncbi.nlm.nih.gov/pubmed/24620624

"the authors intend to present ASIA, or Shoenfeld's syndrome, as an autoimmune syndrome induced by adjuvants"

ASIA

Autoimmune And Inflammatory Disorders Caused By Vaccination

There Are Nearly 100 New Disorders Quietly Affecting 50 Million Americans

An Introduction To The Peer Review
by Jeff Prager

The media claims vaccination is a safe and sound medical science. The peer reviewed literature tells a different story entirely. It's a story of a continuing collection of new discoveries in immunity, autoimmunity, brain chemistry, neurology, virology and vaccinology and including a number of other specialties. Aluminum and mercury injected into the human body are both only recently being investigated by the scientific community for safety and all of the issues surrounding injecting either of these metals are still largely unknown.

Vaccination is a science being applied to each and every one of us very, very liberally and especially so with the vaccine schedule currently approved here in the USA. And we are the single most vaccinated population, by far, on earth. Yet we also have some of the highest rates in the world for the 24 primary and nearly 100 total autoimmune diseases.

Autoimmune Diseases encompass an incredible list of symptoms across an enormous number of widely differing disorders that affect every single human body organ and most often, multiple organs.

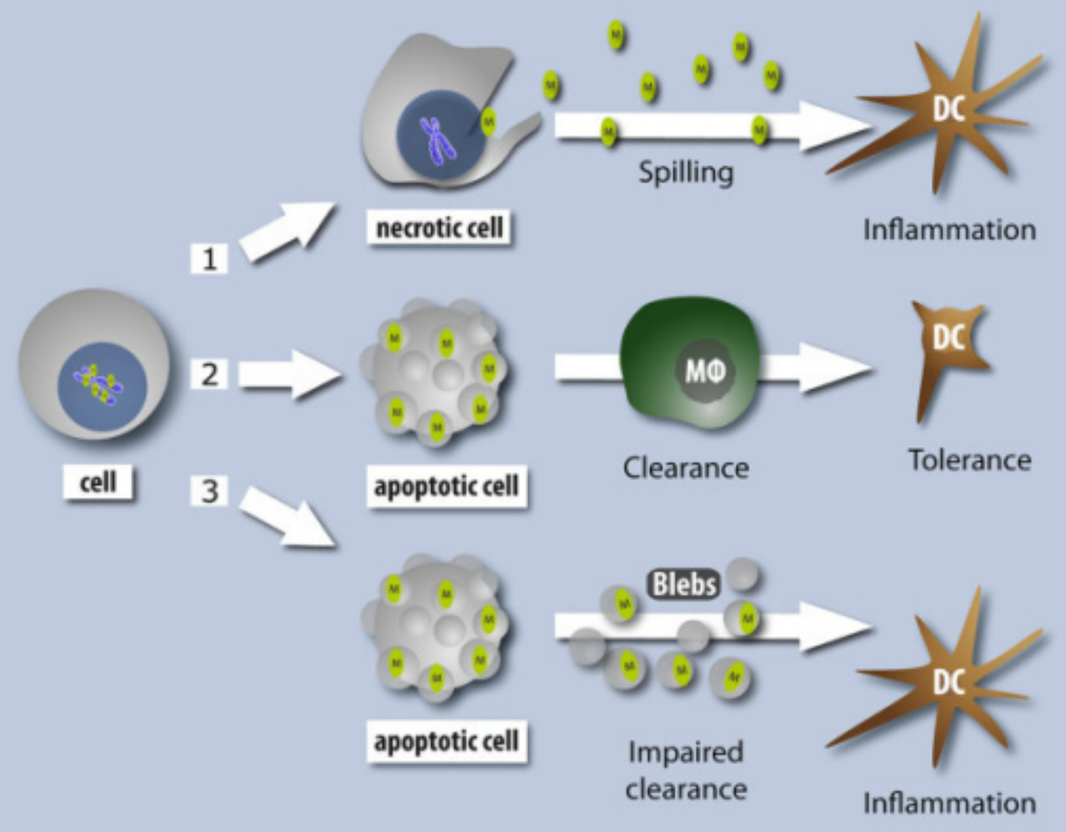
In February 2011 in the Journal of Autoimmunity researcher Yehuda Shoenfeld published 'ASIA' - autoimmune/inflammatory syndrome induced by adjuvants and officially established. coined and defined the acronym ASIA. Shoenfeld said, "*In recent years, four conditions: siliconosis, the Gulf war syndrome (GWS), the macrophagic myofasciitis syndrome (MMF) and post-vaccination phenomena were linked with previous exposure to an adjuvant. Furthermore, these four diseases share a similar complex of signs and symptoms which further support a common denominator. Thus, we review herein the current data regarding the role of adjuvants in the pathogenesis of immune mediated diseases as well as the amassed data regarding each of these four conditions. Relating to the current knowledge we would like to suggest to include these comparable conditions under a common syndrome entitled ASIA*, "*Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants*"."

In early 2013, the authors of a textbook on autoimmune diseases concluded that "*there exists persuasive evidence for ASIA*". As you'll see here, the peer reviewed literature and the scientific community have linked aluminum adjuvants in vaccines directly to various immune and inflammatory disorders in humans and the overwhelming number of separate reports by a variety of researchers paints a worrisome picture indeed. Vaccines are causing epidemics, actually what might even be more accurately described as pandemics, and of the worst kind. Nearly

100 known and suspected Autoimmune and inflammatory diseases affecting 50 million people here in the USA and millions more worldwide makes that inarguable.

In April of 2013, Shoenfeld, along with several other researchers, published once again in Expert Review of Clinical Immunology. The group stated, "*The main substances associated with ASIA are squalene (Gulf War syndrome), aluminum hydroxide (postvaccination phenomena, macrophagic myofasciitis) and silicone with siliconosis. Mineral oil, guaiacol and iodine gadital are also associated with ASIA. The following review describes the wide clinical spectrum and pathogenesis of ASIA including defined autoimmune diseases and nonspecific autoimmune manifestations, as well as the outlook of future research in this field.*"

Since then a variety of researchers, both individuals and groups, have published peer reviewed papers helping the research community better understand the relatively recent phenomenon of ASIA. ASIA encompasses a variety of disease symptoms much like Autistic Spectrum Disorder (ASD) encompasses a variety of symptoms and there is sufficient research evidence, also included here, to assume that aluminum in vaccines causes some symptoms related to both ASIA and Autism Spectrum Disorder in susceptible individuals. This PDF collects the best evidence for these assertions as it relates to Aluminum and vaccination. There are other adjuvant and adjuvant-like components of vaccines (squalene, DNA fragments, Polysorbate 80, MSG, etc) that also cause unusual illnesses in humans and these are not covered here.



Macrophagic Myofasciitis (MMF)

Macrophagic myofasciitis (MMF) was reported in 1998. MMF is characterized by post-vaccination systemic manifestations as well as local-stereotyped and immunologically active lesion in the site of inoculation (deltoid muscle). MMF systemic symptoms included myalgias, which is pain in various muscle groups, arthralgias, which is joint pain, marked asthenia, which is abnormal weakness and lack of energy, muscle weakness, chronic fatigue, and fever.

Recently, studies demonstrate that the local lesion at the site of injection is due to persistence for years of an aluminum (Al(OH)3) adjuvant commonly used in human vaccines. Time elapsed from last immunization with an Aluminum-containing vaccine to muscle biopsy range from 3 months to 8 years; in rare cases, MMF may be diagnosed even 10 years post-vaccination. Observations suggest that aluminum-containing vaccinations may trigger MMF in genetically susceptible subjects carrying the HLA-DRB1*01 gene. Thus, MMF may be defined as an emerging novel condition that may be triggered by exposure to alum-containing vaccines, in patients with a specific genetic background, and this temporal association may be exhibited from a few months up to 10 years, or more, later.

A Macrophage

A macrophage from a mouse stretching its “arms” (pseudopodia) to engulf two particles, possibly pathogens.

Gulf War Syndrome (GWS)

Gulf War syndrome (GWS), also known as Gulf War illness (GWI), is a chronic multisymptom disorder affecting returning military veterans and civilian workers of the 1990–91 Gulf War. A wide range of acute and chronic symptoms have been linked to it, including fatigue, muscle pain, cognitive problems, rashes and diarrhea. Approximately 250,000 of the 697,000 U.S. veterans who served in the 1991 Gulf War are afflicted with enduring chronic multi-symptom illness, a condition with serious consequences. From 1995 to 2005, the health of combat veterans worsened in comparison with non-deployed veterans, with the onset of more new chronic diseases, functional impairment, repeated clinic visits and hospitalizations, chronic fatigue syndrome-like illness, posttraumatic stress disorder, and a greater persistence of adverse health incidents. According to a report by the Iraq and Afghanistan Veterans of America, veterans of Iraq and Afghanistan may also suffer from Gulf War Syndrome. Suggested causes have included depleted uranium, sarin gas, smoke from burning oil wells, vaccinations, combat stress and psychological factors.

Medical ailments associated with Gulf War syndrome have been recognized by both the Department of Defense and the Department of Veterans Affairs although there is no formal definition of the term “Gulf War syndrome” or “Gulf War illnesses”

During Operation Desert Storm, 41% of U.S. combat soldiers and 75% of UK combat soldiers were vaccinated against anthrax. Reactions included local skin irritation, some lasting for weeks or months. While the Food and Drug Administration (FDA) approved the vaccine, it never went through large-scale clinical trials, unlike most other vaccines in the United States.

Recent studies have demonstrated the vaccine is highly reactogenic and causes motor neuron death in mice and the peer reviewed literature herein links all aluminum-containing vaccines to Gulf War Syndrome. Nevertheless, the Committee on Gulf War Veterans’ Illnesses concluded that the vaccine is not a likely cause of Gulf War illness for most ill veterans.

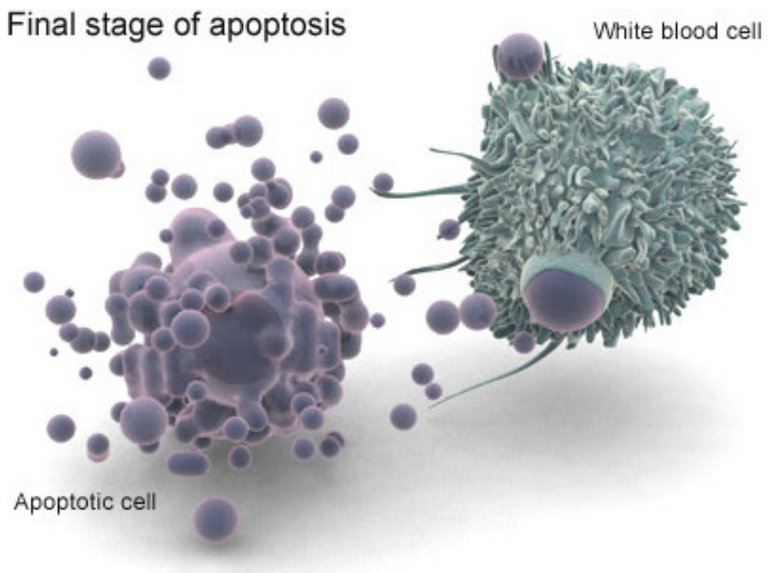
A fuller understanding of immune function in ill Gulf War veterans is needed, particularly in veteran subgroups with different clinical characteristics and exposure histories. It is also important to determine the extent to which identified immune perturbations may be associated with altered neurological and endocrine processes that are associated with immune regulation. Very limited cancer data have been reported for U.S. Gulf War veterans in general, and no published research on cases occurring after 1999. Because of the extended latency periods associated with most cancers, it is important that cancer information be brought up to date and that cancer rates be assessed in Gulf War veterans on an ongoing basis. In addition, cancer rates should be evaluated in relation to identifiable exposure and location subgroups.

On March 14, 2014, Representative Mike Coffman introduced the Gulf War Health Research Reform Act of 2014 (H.R. 4261; 113th Congress) into the United States House of Representatives. The bill would alter the relationship between the Research Advisory Committee on Gulf War Illnesses (RAC) and the United States Department of Veterans Affairs (VA). The bill would make the RAC an independent organization within the VA, require that a majority of the RAC’s members be appointed by Congress instead of the VA, and state that the RAC can release its reports without needing prior approval from the Secretary of Veterans Affairs. The RAC is responsible for investigating Gulf War syndrome.

In the year prior to the consideration of this bill, the VA and the RAC were at odds with one another. The VA replaced all but one of the members of the RAC, removed some of their supervisory tasks, and ultimately tried to influence the board to decide that stress, rather than biology was the cause of Gulf War syndrome, and told the RAC that it could not publish reports without permission.

The RAC was originally created in 1997, after Congress decided that the VA’s research into the issue was flawed, and focused on psychological causes, while mostly ignoring biological ones. The bill still languishes in committee. Here in this PDF we provide the data in peer reviewed reports and studies that links the aluminum adjuvant in vaccines to Gulf War Syndrome.

Apoptosis & Necrosis

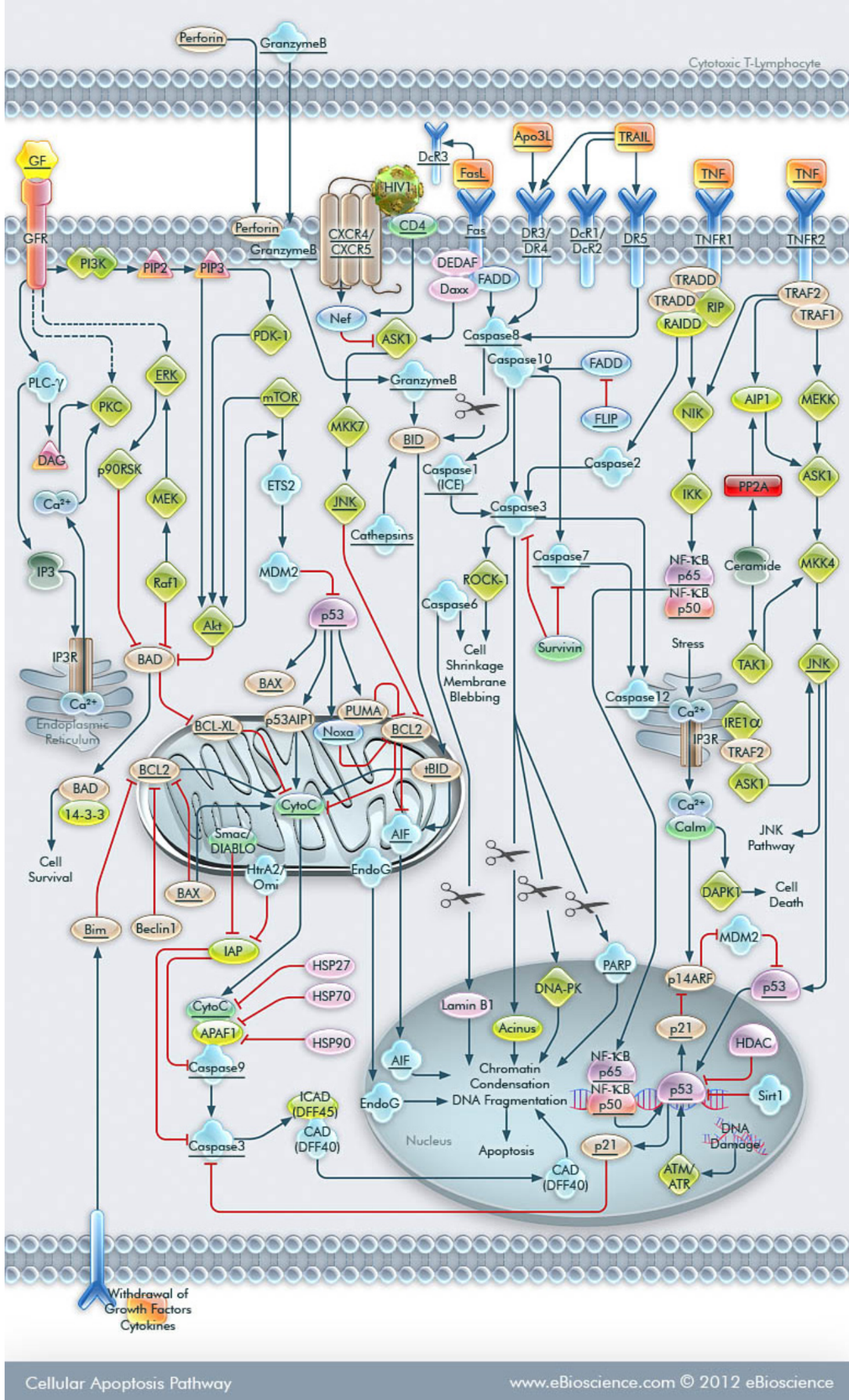


Apoptosis is the process of programmed cell death that may occur in multicellular organisms. Biochemical events lead to characteristic cell changes (morphology) and death. These changes include blebbing, cell shrinkage, nuclear fragmentation, chromatin condensation, chromosomal DNA fragmentation, and global mRNA decay.

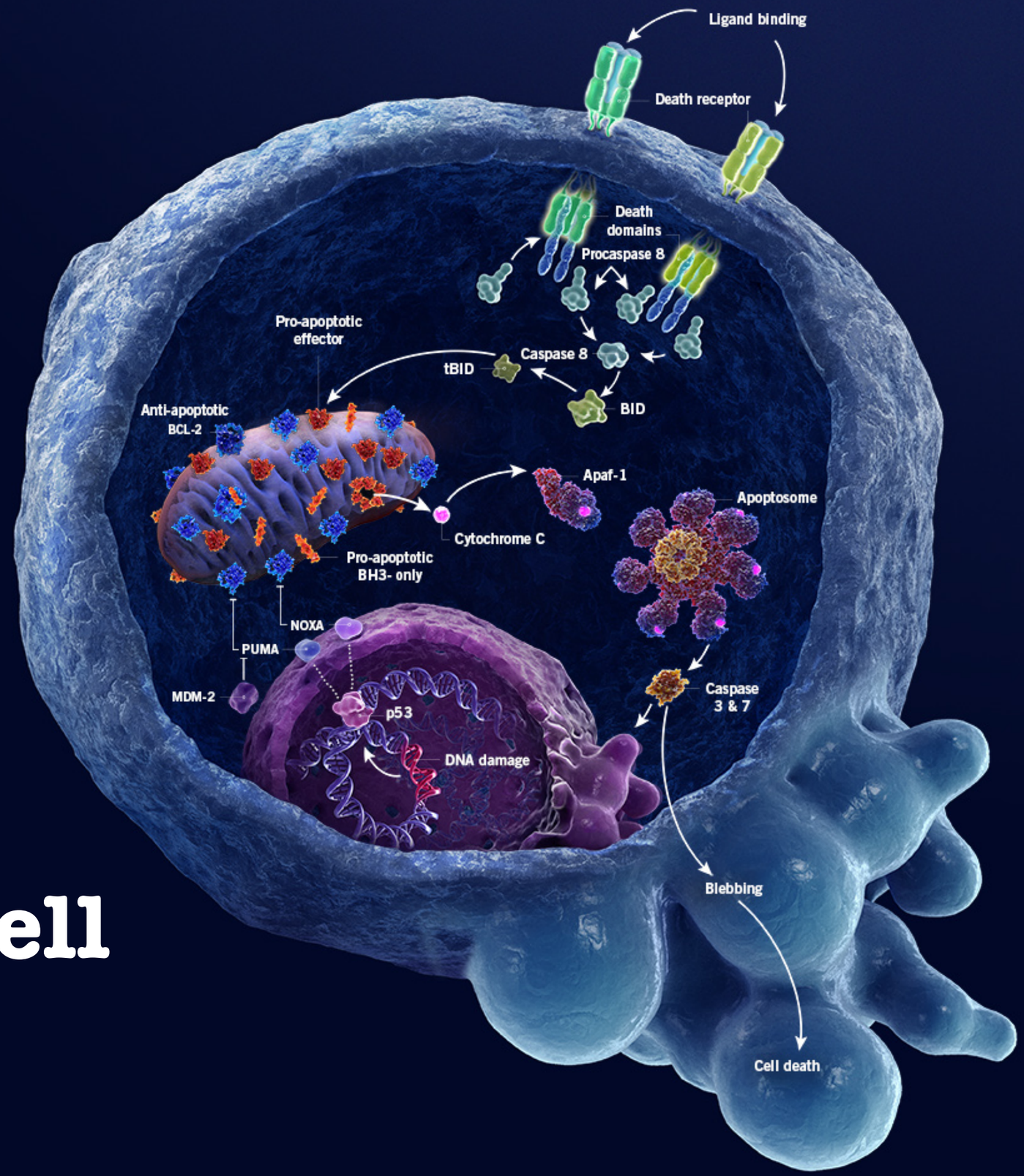
In contrast to necrosis, which is a form of traumatic cell death that results from acute cellular injury, apoptosis is a highly regulated and controlled process that confers advantages during an organism's lifecycle. For example, the separation of fingers and toes in a developing human embryo occurs because cells between the digits undergo apoptosis. Unlike necrosis, apoptosis produces cell fragments called apoptotic bodies that phagocytic cells are able to engulf and quickly remove before the contents of the cell can spill out onto surrounding cells and cause damage.

Between 50 and 70 billion cells die each day due to apoptosis in the average human adult. For an average child between the ages of 8 and 14, approximately 20 billion to 30 billion cells die a day. Research in and around apoptosis has increased substantially since the early 1990s. In addition to its importance as a biological phenomenon, defective apoptotic processes have been implicated in a wide variety of diseases. Excessive apoptosis causes atrophy, whereas an insufficient amount results in uncontrolled cell proliferation, such as cancer.

The extraordinary complexities associated with cellular apoptosis are diagrammed at right and while it's not necessary to understand the process, it's important to recognize the intricate and elaborate system that the human being is and how many different junctures, intersections and opportunities there are for things to go wrong within the human body and for those differences to manifest as disease and disorder. We're learning that a "one-size-fits-all" vaccination policy will, by its very nature, cause severe and long-lasting harm to many of its victims and it's a hard lesson to learn.



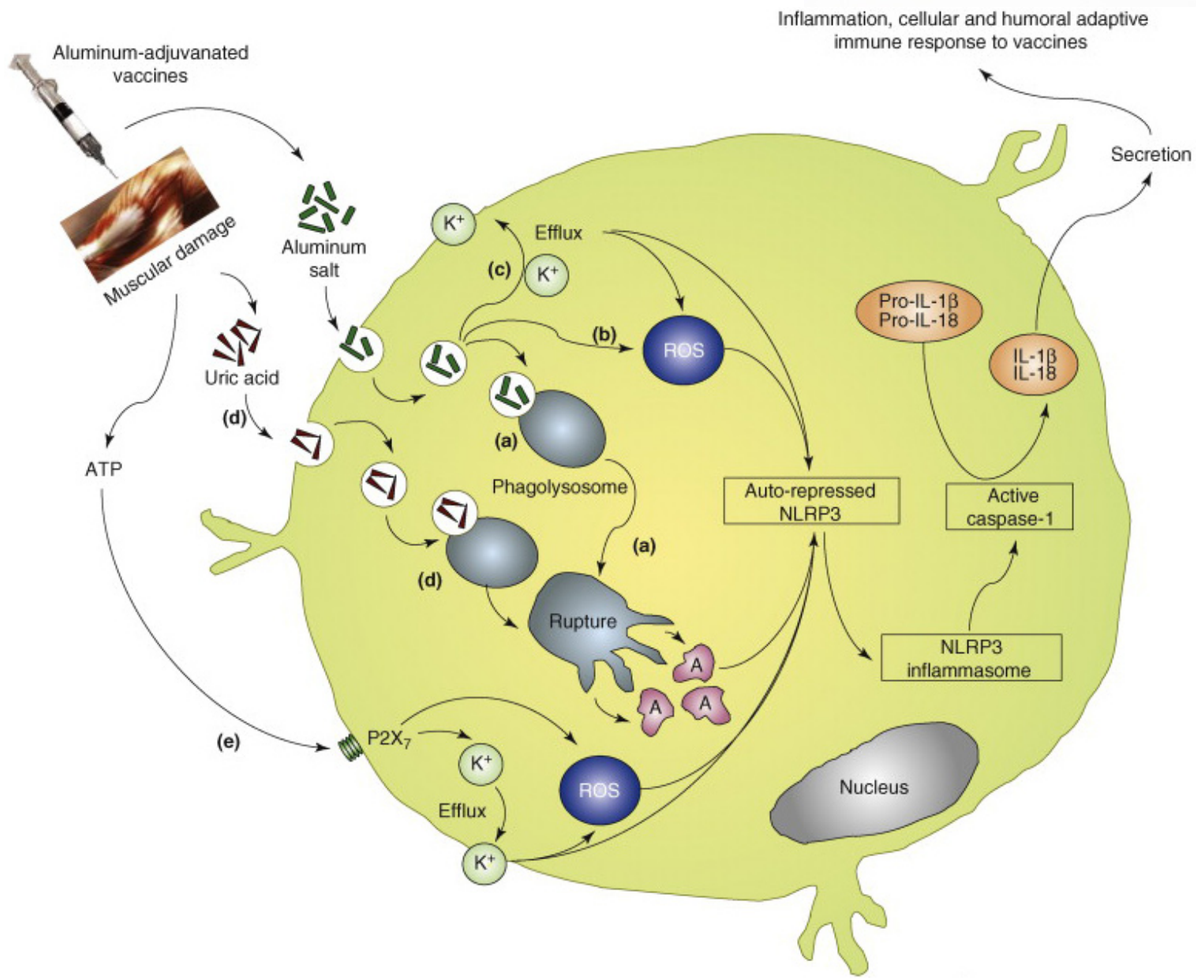
The Death Of A Cell



Vaccines

How They Work and Don't...

Pictured below is a very basic diagram showing the theory behind vaccination. Although vaccines do seem to work to some degree for a number of people, current research—peer reviewed reports and studies in the fields of immunology, virology, vaccinology, neurology and biology—proves not how much we understand about the science that involve vaccination, but how truly little we really know. If the research in the 100+ studies reproduced here is even



marginally accurate then we've overdosed generations with a known neurotoxin that is recognized to bioaccumulate in the brain and cause a variety of debilitating disorders that could manifest anytime during our lifetimes, immediately or decades in the future. Not only that, many of our vaccines confer limited population-wide immunity. In other words, for many of us they actually don't work very well at all and for many more of us they don't work for very long.

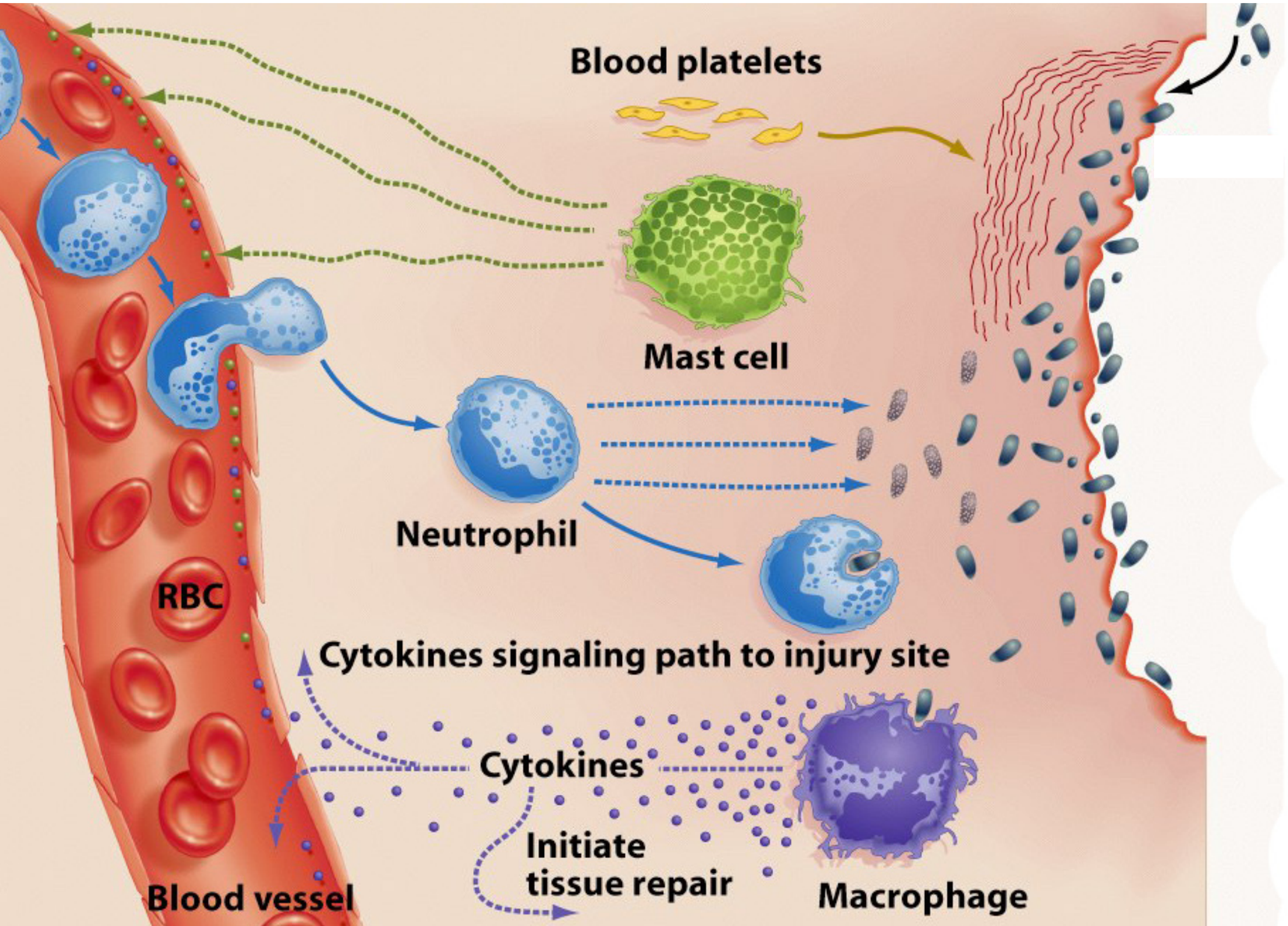
The sheer complexity of effectively creating human immunity, the significant differences between cell-mediated immunity and humoral immunity, the extraordinary intricacies in the innate and adaptive immune systems and the synergy between the several ingredients in vaccines, other drugs, diet (vitamin and mineral body content), genetic predispositions and environmental contamination (things like lead, glyphoste, cadmium, chloride, fluoride, cigarette smoke, car exhaust, etc.) is not only not known or understood but likely never will be. There are far too many synergies going on to even begin to explore them properly.

We're only just now beginning to question previously held beliefs and investigate the affects of injecting aluminum hydroxide and other aluminum salts, squalene, thimerosal and other adjuvants into the human body after assuming for decades that, for example, injecting aluminum was safe. We're slowly finding out now that injecting aluminum is anything but safe.

And we're learning more every day about the serious drawbacks involved with injecting these adjuvants into the human body. And believe me, there's no rush to research by the scientific community. Even in the dearth of current data, the writing is on the wall. Thimerosal and aluminum salts are not well tolerated by humans and are known to cause a myriad of neurological and other debilitating disorders, especially in those that are variously genetically susceptible. It turns out that vaccination saved us from 8 or 10 tolerable illnesses and created 100s of intolerable disorders in their place and that makes sense now. Vaccination is, after all, like a shot in the dark and as it turns out, vaccinations weren't really the panacea they were once thought to be, after all.

The Normal Inflammatory Response

... With Autoimmune Diseases The Inflammatory Response May Never Turn Off ...



What Happens?

1. Bacteria and other pathogens that inhabit your skin microbiome will enter the wound.

2. Platelets from your blood release blood-clotting proteins at the wound site.

3. Mast cells secrete factors that mediate dilation and constriction of blood vessels. Delivery of blood, plasma, and cells to injured area increases.

4. Neutrophils secrete factors that kill and degrade pathogens.

5. Neutrophils and macrophages remove pathogens by phagocytosis

6. Macrophages secrete cytokines, which attract immune system cells to the site and activate cells involved in tissue repair.

7. Inflammatory response continues until the foreign material is eliminated and the wound is repaired.

From the Journal Presse Medicale • February 2000

Macrophagic myofasciitis. Study and Research Group on Acquired and Dysimmunity-related muscular diseases (GERMMAD)

Chérin P, Laforêt P, Ghérardi RK, Authier FJ, Maisonobe T,
Coquet M, Mussini JM, Pellissier JF, Eymard B, Herson S.

Service de Médecine Interne, Groupe Hospitalier Pitié-Salpêtrière, Paris
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Abstract

MACROPHAGIC MYOFASCIITIS

A most unusual inflammatory myopathy, first described by Germmad had been reported with increasing frequency since 1993 in the leading French myopathology centers. We present our experience with this new disease: macrophagic myofasciitis.

CLINICAL FEATURES

By November 1999, 70 cases of macrophagic myofasciitis had been recorded since our first description. The first 22 patients (sex ratio M/F = 1:3) referred with the presumptive diagnosis of polymyositis (n = 11), polymyalgia rheumatica (n = 5), mitochondrial cytopathy (n = 4), and congenital myopathy or muscle dystrophy (n = 1 each). Symptoms included myalgia (91%), anthralgia (68%), marked asthenia (55%), muscle weakness (45%), and fever (32%).

LABORATORY FINDINGS

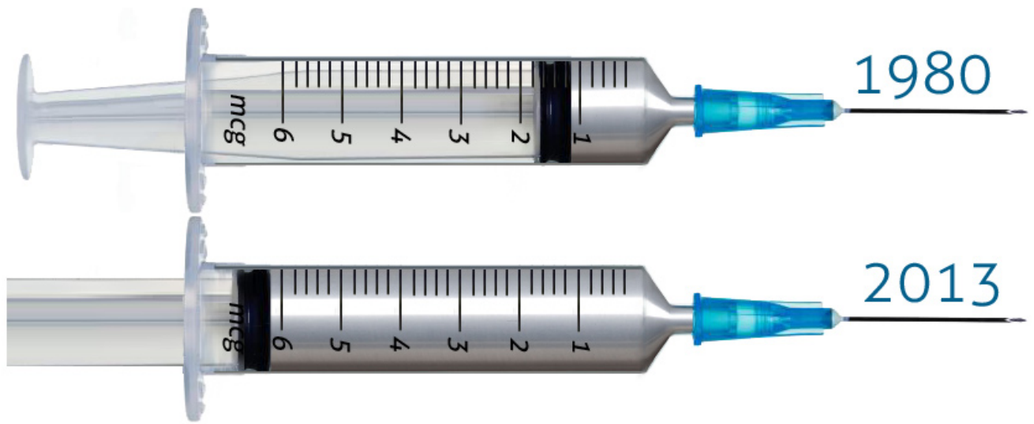
Abnormal laboratory findings included elevated CK levels (50%), markedly increased erythrocyte sedimentation rate (37%), and myopathic EMG (35%). Muscle biopsy showed a unique myopathological pattern characterized by: i) centripetal infiltration of epimysium, perimysium and perifascicular endomysium by sheets of large cells of the monocyte/macrophage lineage (CD68+, CD1a-, S100-, with a PAS-positive content; ii) absence of necrosis, of both epithelioid and giant cells, and of mitotic figures; iii) presence of occasional CD8+ T-cells; iv) inconspicuous muscle fiber damage. The picture was easily distinguishable from sarcoid myopathy and fasciitis-panniculitis syndromes. The infectious diseases know to be associated with reactive histiocytes, including Whippleís disease, Mycobacterium avium intracellulare infection and malakoplakia, could not be documented. Patients improved under corticosteroid therapy and/or immunomodulatory therapeutic

CONCLUSION

A new inflammatory muscle disorder, characterized by a distinctive pathological pattern of macrophagic myofasciitis is emerging in France

http://www.ncbi.nlm.nih.gov/pubmed/10705901

“A new inflammatory muscle disorder characterized by a distinctive pathological pattern of macrophagic myofasciitis is emerging in France”



From the Journal Immunotherapy • January 2014

Are there negative Central Nervous System impacts of aluminum adjuvants used in vaccines and immunotherapy?

Shaw CA1, Li D, Tomljenovic L.
Neural Dynamics Research Group,
828 W. 10th Ave, Vancouver, BC, V5Z 1L8, Canada.

Abstract

In spite of a common view that aluminum (Al) salts are inert and therefore harmless as vaccine adjuvants or in immunotherapy, the reality is quite different. In the following article we briefly review the literature on Al neurotoxicity and the use of Al salts as vaccine adjuvants and consider not only direct toxic actions on the nervous system, but also the potential impact for triggering autoimmunity. Autoimmune and inflammatory responses affecting the CNS appear to underlie some forms of neurological disease, including developmental disorders. Al has been demonstrated to impact the CNS at every level, including by changing gene expression. These outcomes should raise concerns about the increasing use of Al salts as vaccine adjuvants and for the application as more general immune stimulants.

http://www.ncbi.nlm.nih.gov/pubmed/25428645

> “These outcomes should raise concerns about the increasing use of Al salts as vaccine adjuvants”

From the Journal Lupus • September 2015

Human adjuvant-related syndrome or autoimmune/inflammatory syndrome induced by adjuvants. Where have we come from? Where are we going? A proposal for new diagnostic criteria.

Alijotas J-Reig J.

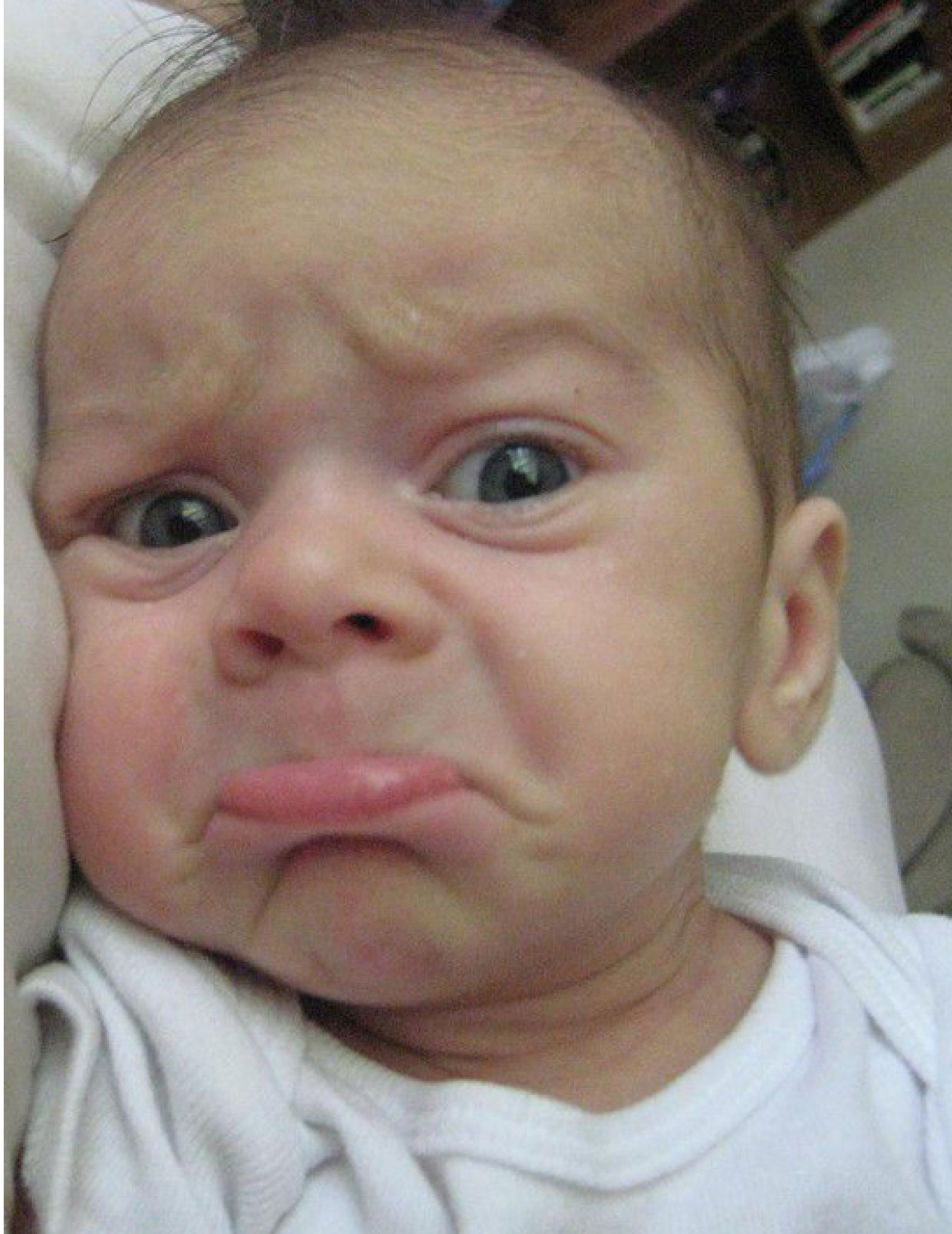
Systemic Autoimmune Disease Unit, Department of Internal Medicine I,
Vall d'Hebron UniversityHospital, Faculty of Medicine, Universitat Autonoma, Barcelona, Spain
16297jar@comb.es and jalijotas@vhebron.net

Abstract

In 1964, Miyoshi reported a series of patients with diverse symptoms after receiving treatment with silicone or paraffin fillers. Miyoshi named this condition 'human adjuvant disease'. Since then, the literature has been flooded with case reports and case series of granulomatous and systemic autoimmune disorders related to vaccines, infection or other adjuvants such as silicone and other biomaterials. A new term -autoimmune/inflammatory syndrome induced by adjuvants - has recently been coined for a process that includes several clinical features previously described by Miyoshi plus other clinical and laboratory parameters related to exposure to diverse external stimuli. Disorders such as siliconosis, Gulf War syndrome, macrophagic myofasciitis syndrome, sick building syndrome and post-vaccination syndrome have been included in autoimmune/inflammatory syndrome induced by adjuvants. Disorders such as Spanish toxic oil syndrome and Ardystil syndrome could also be included. Furthermore, biomaterials other than silicone should also be considered as triggering factors for these adjuvant-related syndromes. New diagnostic criteria in this field have been proposed. Nevertheless, many of these criteria are too subjective, leading to some patients being diagnosed with chronic fatigue syndrome or other 'central sensitization syndromes'. Diagnostic criteria based only on objective clinical and laboratory data to be further discussed and validated are proposed herein.

http://www.ncbi.nlm.nih.gov/pubmed/25813870

"Since then, the literature has been flooded with case reports and case series of granulomatous and systemic autoimmune disorders related to vaccines ..."



From the Journal Immunological Research • July 2013

Aluminum in the central nervous system (CNS): toxicity in humans and animals, vaccine adjuvants, and autoimmunity

Shaw CA, Tomljenovic L.

Abstract

We have examined the neurotoxicity of aluminum in humans and animals under various conditions, following different routes of administration, and provide an overview of the various associated disease states. The literature demonstrates clearly negative impacts of aluminum on the nervous system across the age span. In adults, aluminum exposure can lead to apparently age-related neurological deficits resembling Alzheimer's and has been linked to this disease and to the Guamanian variant, ALS-PDC. Similar outcomes have been found in animal models. In addition, injection of aluminum adjuvants in an attempt to model Gulf War syndrome and associated neurological deficits leads to an ALS phenotype in young male mice. In young children, a highly significant correlation exists between the number of pediatric aluminum-adjuvanted vaccines administered and the rate of autism spectrum disorders. Many of the features of aluminum-induced neurotoxicity may arise, in part, from autoimmune reactions, as part of the ASIA syndrome.

http://www.ncbi.nlm.nih.gov/pubmed/23609067

"In young children, a highly significant correlation exists between the number of pediatric aluminum-adjuvanted vaccines administered and the rate of autism spectrum disorders. Many of the features of aluminum-induced neurotoxicity may arise, in part, from autoimmune reactions, as part of the ASIA syndrome"

From the Journal Inorganic Biochemistry
November 2013

Administration of aluminium to neonatal mice in vaccine-relevant amounts is associated with adverse long term neurological outcomes

Shaw CA, Li Y, Tomljenovic L.

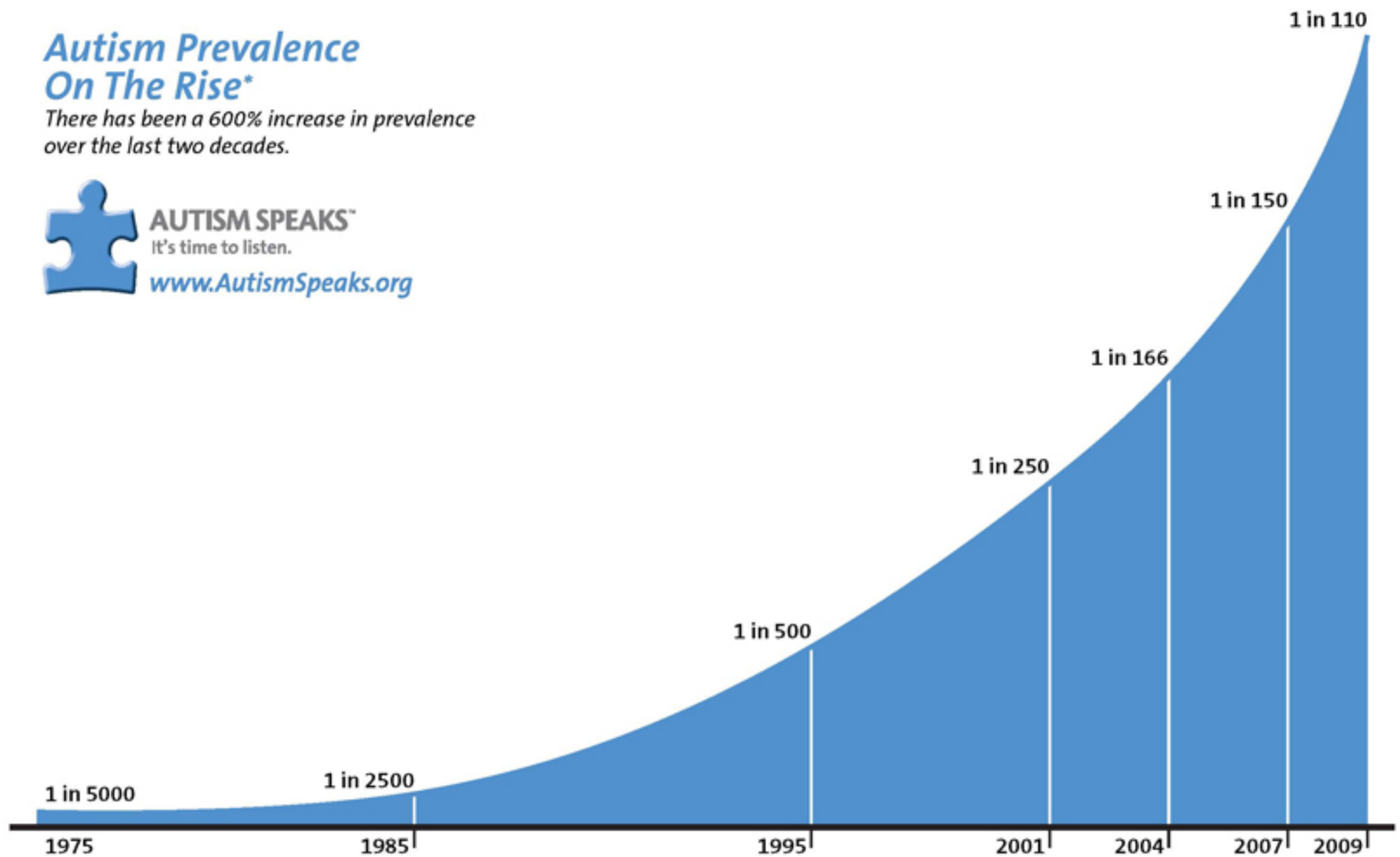
Dept. of Ophthalmology and Visual Sciences,
Program in Experimental Medicine,
Program in Neuroscience,
University of British Columbia, Vancouver, Canada
Electronic address: cashawlab@gmail.com.

Abstract

Our previous ecological studies of autism spectrum disorder (ASD) has demonstrated a correlation between increasing ASD rates and aluminium (Al) adjuvants in common use in paediatric vaccines in several Western countries. The correlation between ASD rate and Al adjuvant amounts appears to be dose-dependent and satisfies 8 of 9 Hill criteria for causality. We have now sought to provide an animal model to explore potential behavioural phenotypes and central nervous system (CNS) alterations using s.c. injections of Al hydroxide in early postnatal CD-1 mice of both sexes. Injections of a "high" and "low" Al adjuvant levels were designed to correlate to either the U.S. or Scandinavian paediatric vaccine schedules vs. control saline-injected mice. Both male and female mice in the "high Al" group showed significant weight gains following treatment up to sacrifice at 6 months of age. Male mice in the "high Al" group showed significant changes in light-dark box tests and in various measures of behaviour in an open field. Female mice showed significant changes in the light-dark box at both doses, but no significant changes in open field behaviours. These current data implicate Al injected in early postnatal life in some CNS alterations that may be relevant for a better understanding of the aetiology of ASD.

http://www.ncbi.nlm.nih.gov/pubmed/23932735

"These current data implicate Aluminum injected in early postnatal life in some Central Nervous System alterations that may be relevant for a better understanding of the etiology of Autistic Spectrum Disorder"



From the Journal of Trace Elements in Medicine and Biology
October 2012

Aluminium overload after 5 years in skin biopsy following post-vaccination with subcutaneous pseudolymphoma

Guillard O1, Fauconneau B, Pineau A,
Marrauld A, Bellocq JP, Chenard MP.

CHU Poitiers, Department of Biochemistry, Poitiers, France.
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Abstract

Aluminium hydroxide is used as an effective adjuvant in a wide range of vaccines for enhancing immune response to the antigen. The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines. The aim of this study is to verify if the subcutaneous pseudolymphoma observed in this patient in the site of vaccine injection is linked to an aluminium overload. Many years after vaccination, a subcutaneous nodule was discovered in a 45-year-old woman with subcutaneous pseudolymphoma. In skin biopsy at the injection site for vaccines, aluminium (Al) deposits are assessed by Morin stain and quantification of Al is performed by Zeeman Electrothermal Atomic Absorption Spectrophotometry. Morin stain shows Al deposits in the macrophages, and Al assays (in µg/g, dry weight) were 768.10±18 for the patient compared with the two control patients, 5.61±0.59 and 9.13±0.057. Given the pathology of this patient and the high Al concentration in skin biopsy, the authors wish to draw attention when using the Al salts known to be particularly effective as adjuvants in single or repeated vaccinations. The possible release of Al may induce other pathologies ascribed to the well-known toxicity of this metal.

http://www.ncbi.nlm.nih.gov/pubmed/22425036

“Aluminium hydroxide is used as an effective adjuvant in a wide range of vaccines for enhancing immune response to the antigen.

The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines”

From the Journal Lupus • February 2012

Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations

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Abstract

Immune challenges during early development, including those vaccine-induced, can lead to permanent detrimental alterations of the brain and immune function. Experimental evidence also shows that simultaneous administration of as little as two to three immune adjuvants can overcome genetic resistance to autoimmunity. In some developed countries, by the time children are 4 to 6 years old, they will have received a total of 126 antigenic compounds along with high amounts of aluminum (Al) adjuvants through routine vaccinations. According to the US Food and Drug Administration, safety assessments for vaccines have often not included appropriate toxicity studies because vaccines have not been viewed as inherently toxic. Taken together, these observations raise plausible concerns about the overall safety of current childhood vaccination programs. When assessing adjuvant toxicity in children, several key points ought to be considered: (i) infants and children should not be viewed as "small adults" with regard to toxicological risk as their unique physiology makes them much more vulnerable to toxic insults; (ii) in adult humans Al vaccine adjuvants have been linked to a variety of serious autoimmune and inflammatory conditions (i.e., "ASIA"), yet children are regularly exposed to much higher amounts of Al from vaccines than adults; (iii) it is often assumed that peripheral immune responses do not affect brain function. However, it is now clearly established that there is a bidirectional neuro-immune cross-talk that plays crucial roles in immunoregulation as well as brain function. In turn, perturbations of the neuro-immune axis have been demonstrated in many autoimmune diseases encompassed in "ASIA" and are thought to be driven by a hyperactive immune response; and (iv) the same components of the neuro-immune axis that play key roles in brain development and immune function are heavily targeted by Al adjuvants. In summary, research evidence shows that increasing concerns about current vaccination practices may indeed be warranted. Because children may be most at risk of vaccine-induced complications, a rigorous evaluation of the vaccine-related adverse health impacts in the pediatric population is urgently needed.

http://www.ncbi.nlm.nih.gov/pubmed/22235057

"... the same components of the neuro-immune axis that play key roles in brain development and immune function are heavily targeted by Al [aluminum] adjuvants.

In summary, research evidence shows that increasing concerns about current vaccination practices may indeed be warranted. Because children may be most at risk of vaccine induced complications, a rigorous evaluation of the vaccine related adverse health impacts in the pediatric population is urgently needed"

From the Journal Revue Neurologique (Paris) • February 2003

Lessons from macrophagic myofasciitis: towards definition of a vaccine adjuvant-related syndrome

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Abstract

Macrophagic myofasciitis is a condition first reported in 1998, which cause remained obscure until 2001. Over 200 definite cases have been identified in France, and isolated cases have been recorded in other countries. The condition manifests by diffuse myalgias and chronic fatigue, forming a syndrome that meets both Center for Disease Control and Oxford criteria for the so-called chronic fatigue syndrome in about half of patients. One third of patients develop an autoimmune disease, such as multiple sclerosis. Even in the absence of overt autoimmune disease they commonly show subtle signs of chronic immune stimulation, and most of them are of the HLADRB1*01 group, a phenotype at risk to develop polymyalgia rheumatica and rheumatoid arthritis. Macrophagic myofasciitis is characterized by a stereotyped and immunologically active lesion at deltoid muscle biopsy. Electron microscopy, microanalytical studies, experimental procedures, and an epidemiological study recently demonstrated that the lesion is due to persistence for years at site of injection of an aluminum adjuvant used in vaccines against hepatitis B virus, hepatitis A virus, and tetanus toxoid. Aluminum hydroxide is known to potently stimulate the immune system and to shift immune responses towards a Th-2 profile. It is plausible that persistent systemic immune activation that fails to switch off represents the pathophysiologic basis of chronic fatigue syndrome associated with macrophagic myofasciitis, similarly to what happens in patients with post-infectious chronic fatigue and possibly idiopathic chronic fatigue syndrome. Therefore, the WHO recommended an epidemiological survey, currently conducted by the French agency AFSSAPS, aimed at substantiating the possible link between the focal macrophagic myofasciitis lesion (or previous immunization with aluminium-containing vaccines) and systemic symptoms. Interestingly, special emphasis has been put on Th-2 biased immune responses as a possible explanation of chronic fatigue and associated manifestations known as the Gulf war syndrome. Results concerning macrophagic myofasciitis may well open new avenues for etiologic investigation of this syndrome. Indeed, both type and structure of symptoms are strikingly similar in Gulf war veterans and patients with macrophagic myofasciitis. Multiple vaccinations performed over a short period of time in the Persian gulf area have been recognized as the main risk factor for Gulf War syndrome. Moreover, the war vaccine against anthrax, which is administered in a 6-shot regimen and seems to be crucially involved, is adjuvanted by aluminium hydroxide and, possibly, squalene, another Th-2 adjuvant. If safety concerns about long-term effects of aluminium hydroxide are confirmed it will become mandatory to propose novel and alternative vaccine adjuvants to rescue vaccine-based strategies and the enormous benefit for public health they provide worldwide.

http://www.ncbi.nlm.nih.gov/pubmed/12660567

“Multiple vaccinations performed over a short period of time in the Persian gulf area have been recognized as the main risk factor for Gulf War syndrome”

From the Journal Inorganic Biochemistry • November 2009

Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration

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Abstract

Gulf War Syndrome is a multi-system disorder afflicting many veterans of Western armies in the 1990-1991 Gulf War. A number of those afflicted may show neurological deficits including various cognitive dysfunctions and motor neuron disease, the latter expression virtually indistinguishable from classical amyotrophic lateral sclerosis (ALS) except for the age of onset. This ALS "cluster" represents the second such ALS cluster described in the literature to date. Possible causes of GWS include several of the adjuvants in the anthrax vaccine and others. The most likely culprit appears to be aluminum hydroxide. In an initial series of experiments, we examined the potential toxicity of aluminum hydroxide in male, outbred CD-1 mice injected subcutaneously in two equivalent-to-human doses. After sacrifice, spinal cord and motor cortex samples were examined by immunohistochemistry. Aluminum-treated mice showed significantly increased apoptosis of motor neurons and increases in reactive astrocytes and microglial proliferation within the spinal cord and cortex. Morin stain detected the presence of aluminum in the cytoplasm of motor neurons with some neurons also testing positive for the presence of hyper-phosphorylated tau protein, a pathological hallmark of various neurological diseases, including Alzheimer's disease and frontotemporal dementia. A second series of experiments was conducted on mice injected with six doses of aluminum hydroxide. Behavioural analyses in these mice revealed significant impairments in a number of motor functions as well as diminished spatial memory capacity. The demonstrated neurotoxicity of aluminum hydroxide and its relative ubiquity as an adjuvant suggest that greater scrutiny by the scientific community is warranted.

http://www.ncbi.nlm.nih.gov/pubmed/19740540

"Behavioural analyses in these mice revealed significant impairments in a number of motor functions as well as diminished spatial memory capacity. The demonstrated neurotoxicity of aluminum hydroxide and its relative ubiquity as an adjuvant suggest that greater scrutiny by the scientific community is warranted"

From the Journal Inorganic Biochemistry. • November 2012

Do aluminum vaccine adjuvants contribute to the rising prevalence of autism?

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Abstract

Autism spectrum disorders (ASD) are serious multisystem developmental disorders and an urgent global public health concern. Dysfunctional immunity and impaired brain function are core deficits in ASD. Aluminum (Al), the most commonly used vaccine adjuvant, is a demonstrated neurotoxin and a strong immune stimulator. Hence, adjuvant Al has the potential to induce neuroimmune disorders. When assessing adjuvant toxicity in children, two key points ought to be considered: (i) children should not be viewed as "small adults" as their unique physiology makes them much more vulnerable to toxic insults; and (ii) if exposure to Al from only few vaccines can lead to cognitive impairment and autoimmunity in adults, is it unreasonable to question whether the current pediatric schedules, often containing 18 Al adjuvanted vaccines, are safe for children? By applying Hill's criteria for establishing causality between exposure and outcome we investigated whether exposure to Al from vaccines could be contributing to the rise in ASD prevalence in the Western world. Our results show that: (i) children from countries with the highest ASD prevalence appear to have the highest exposure to Al from vaccines; (ii) the increase in exposure to Al adjuvants significantly correlates with the increase in ASD prevalence in the United States observed over the last two decades (Pearson $r=0.92$, $p<0.0001$); and (iii) a significant correlation exists between the amounts of Al administered to preschool children and the current prevalence of ASD in seven Western countries, particularly at 3-4 months of age (Pearson $r=0.89$-0.94, $p=0.0018$-0.0248). The application of the Hill's criteria to these data indicates that the correlation between Al in vaccines and ASD may be causal. Because children represent a fraction of the population most at risk for complications following exposure to Al, a more rigorous evaluation of Al adjuvant safety seems warranted.

http://www.ncbi.nlm.nih.gov/pubmed/22099159

"... if exposure to Al [aluminum] from only a few vaccines can lead to cognitive impairment and autoimmunity in adults, is it unreasonable to question whether the current pediatric schedules, often containing 18 Al [aluminum] adjuvanted vaccines, are safe for children? The application of the Hill's criteria to these data indicates that the correlation between Al in vaccines and Autistic Spectrum Disorder may be causal. Because children represent a fraction of the population most at risk for complications following exposure to Al, a more rigorous evaluation of Al adjuvant safety seems warranted"

From the Journal Neuromolecular Medicine • 2007

Aluminum adjuvant linked to Gulf War illness induces motor neuron death in mice

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Abstract

Gulf War illness (GWI) affects a significant percentage of veterans of the 1991 conflict, but its origin remains unknown. Associated with some cases of GWI are increased incidences of amyotrophic lateral sclerosis and other neurological disorders. Whereas many environmental factors have been linked to GWI, the role of the anthrax vaccine has come under increasing scrutiny. Among the vaccine's potentially toxic components are the adjuvants aluminum hydroxide and squalene. To examine whether these compounds might contribute to neuronal deficits associated with GWI, an animal model for examining the potential neurological impact of aluminum hydroxide, squalene, or aluminum hydroxide combined with squalene was developed. Young, male colony CD-1 mice were injected with the adjuvants at doses equivalent to those given to US military service personnel. All mice were subjected to a battery of motor and cognitive-behavioral tests over a 6-mo period postinjections. Following sacrifice, central nervous system tissues were examined using immunohistochemistry for evidence of inflammation and cell death. Behavioral testing showed motor deficits in the aluminum treatment group that expressed as a progressive decrease in strength measured by the wire-mesh hang test (final deficit at 24 wk; about 50%). Significant cognitive deficits in water-maze learning were observed in the combined aluminum and squalene group (4.3 errors per trial) compared with the controls (0.2 errors per trial) after 20 wk. Apoptotic neurons were identified in aluminum-injected animals that showed significantly increased activated caspase-3 labeling in lumbar spinal cord (255%) and primary motor cortex (192%) compared with the controls. Aluminum-treated groups also showed significant motor neuron loss (35%) and increased numbers of astrocytes (350%) in the lumbar spinal cord. The findings suggest a possible role for the aluminum adjuvant in some neurological features associated with GWI and possibly an additional role for the combination of adjuvants.

http://www.ncbi.nlm.nih.gov/pubmed/17114826

"The findings suggest a possible role for the aluminum adjuvant in some neurological features associated with Gulf War Illness and possibly an additional role for the combination of adjuvants"

From the Journal Medical Hypotheses • 2009

A role for the body burden of aluminium in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome

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Abstract

Macrophagic myofasciitis and chronic fatigue syndrome are severely disabling conditions which may be caused by adverse reactions to aluminium-containing adjuvants in vaccines. While a little is known of disease aetiology both conditions are characterised by an aberrant immune response, have a number of prominent symptoms in common and are coincident in many individuals. Herein, we have described a case of vaccine-associated chronic fatigue syndrome and macrophagic myofasciitis in an individual demonstrating aluminium overload. This is the first report linking the latter with either of these two conditions and the possibility is considered that the coincident aluminium overload contributed significantly to the severity of these conditions in this individual. This case has highlighted potential dangers associated with aluminium-containing adjuvants and we have elucidated a possible mechanism whereby vaccination involving aluminium-containing adjuvants could trigger the cascade of immunological events which are associated with autoimmune conditions including chronic fatigue syndrome and macrophagic myofasciitis.

http://www.ncbi.nlm.nih.gov/pubmed/19004564

“This case has highlighted potential dangers associated with aluminium-containing adjuvants and we have elucidated a possible mechanism whereby vaccination involving aluminium-containing adjuvants could trigger the cascade of immunological events which are associated with autoimmune conditions including chronic fatigue syndrome and macrophagic myofasciitis”

“At present the choice of adjuvants for human vaccination reflects a compromise between a requirement for adjuvanticity and an acceptable low level of side effects...”

From the Journal Vaccine • 1993

Adjuvants — a balance between toxicity and adjuvanticity

Gupta RK, Relyveld EH, Lindblad EB, Bizzini B, Ben-Efraim S, Gupta CK.

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Abstract

Adjuvants have been used to augment the immune response in experimental immunology as well as in practical vaccination for more than 60 years. The chemical nature of adjuvants, their mode of action and the profile of their side effects are highly variable. Some of the side effects can be ascribed to an unintentional stimulation of different mechanisms of the immune system whereas others may reflect general adverse pharmacological reactions. The most common adjuvants for human use today are still aluminium hydroxide, aluminium phosphate and calcium phosphate although oil emulsions, products from bacteria and their synthetic derivatives as well as liposomes have also been tested or used in humans. In recent years monophosphoryl lipid A, ISCOMs with Quil-A and Syntex adjuvant formulation (SAF) containing the threonyl derivative of muramyl dipeptide have been under consideration for use as adjuvants in humans. At present the choice of adjuvants for human vaccination reflects a compromise between a requirement for adjuvanticity and an acceptable low level of side effects.

http://www.ncbi.nlm.nih.gov/pubmed/8447157

From the Journal Inorganic Biochemistry • July 2015

Highly delayed systemic translocation of aluminum-based adjuvant in CD1 mice following intramuscular injections

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Abstract

Concerns regarding vaccine safety have emerged following reports of potential adverse events in both humans and animals. In the present study, alum, alum-containing vaccine and alum adjuvant tagged with fluorescent nanodiamonds were used to evaluate i) the persistence time at the injection site, ii) the translocation of alum from the injection site to lymphoid organs, and iii) the behavior of adult CD1 mice following intramuscular injection of alum (400µgAl/kg). Results showed for the first time a strikingly delayed systemic translocation of adjuvant particles. Alum-induced granuloma remained for a very long time in the injected muscle despite progressive shrinkage from day 45 to day 270. Concomitantly, a markedly delayed translocation of alum to the draining lymph nodes, major at day 270 endpoint, was observed. Translocation to the spleen was similarly delayed (highest number of particles at day 270). In contrast to C57BL/6J mice, no brain translocation of alum was observed by day 270 in CD1 mice. Consistently neither increase of Al cerebral content, nor behavioral changes were observed. On the basis of previous reports showing alum neurotoxic effects in CD1 mice, an additional experiment was done, and showed early brain translocation at day 45 of alum injected subcutaneously at 200µgAl/kg. This study confirms the striking biopersistence of alum. It points out an unexpectedly delayed diffusion of the adjuvant in lymph nodes and spleen of CD1 mice, and suggests the importance of mouse strain, route of administration, and doses, for future studies focusing on the potential toxic effects of aluminum-based adjuvants.

http://www.ncbi.nlm.nih.gov/pubmed/26384437

“...an additional experiment was done, and showed early brain translocation at day 45 of alum injected subcutaneously at 200µgAl/kg. This study confirms the striking biopersistence of alum. It points out an unexpectedly delayed diffusion of the adjuvant in lymph nodes and spleen...”

From the Journal Pharmacological Research • August 2015

Vaccines, adjuvants and autoimmunity

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Abstract

Vaccines and autoimmunity are linked fields. Vaccine efficacy is based on whether host immune response against an antigen can elicit a memory T-cell response over time. Although the described side effects thus far have been mostly transient and acute, vaccines are able to elicit the immune system towards an autoimmune reaction. The diagnosis of a definite autoimmune disease and the occurrence of fatal outcome post-vaccination have been less frequently reported. Since vaccines are given to previously healthy hosts, who may have never developed the disease had they not been immunized, adverse events should be carefully accessed and evaluated even if they represent a limited number of occurrences. In this review of the literature, there is evidence of vaccine-induced autoimmunity and adjuvant-induced autoimmunity in both experimental models as well as human patients. Adjuvants and infectious agents may exert their immune-enhancing effects through various functional activities, encompassed by the adjuvant effect. These mechanisms are shared by different conditions triggered by adjuvants leading to the autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome). In conclusion, there are several case reports of autoimmune diseases following vaccines, however, due to the limited number of cases, the different classifications of symptoms and the long latency period of the diseases, every attempt for an epidemiological study has so far failed to deliver a connection. Despite this, efforts to unveil the connection between the triggering of the immune system by adjuvants and the development of autoimmune conditions should be undertaken. Vaccinomics is a field that may bring to light novel customized, personalized treatment approaches in the future.

http://www.ncbi.nlm.nih.gov/pubmed/26275795

“In this review of the literature, there is evidence of vaccine-induced autoimmunity and adjuvant-induced autoimmunity in both experimental models as well as human patients ... leading to the autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome)”

From the Journal Lupus • February 2012

Macrophagic myofasciitis: characterization and pathophysiology

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Abstract

Aluminium oxyhydroxide (alum), a nanocrystalline compound forming agglomerates, has been used in vaccines for its immunological adjuvant effect since 1927. Alum is the most commonly used adjuvant in human and veterinary vaccines, but the mechanisms by which it stimulates immune responses remain incompletely understood. Although generally well tolerated, alum may occasionally cause disabling health problems in presumably susceptible individuals. A small proportion of vaccinated people present with delayed onset of diffuse myalgia, chronic fatigue and cognitive dysfunction, and exhibit very long-term persistence of alum-loaded macrophages at the site of previous intramuscular (i.m.) immunization, forming a granulomatous lesion called macrophagic myofasciitis (MMF). Clinical symptoms associated with MMF are paradigmatic of the recently delineated 'autoimmune/inflammatory syndrome induced by adjuvants' (ASIA). The stereotyped cognitive dysfunction is reminiscent of cognitive deficits described in foundry workers exposed to inhaled Al particles. Alum safety concerns will largely depend on whether the compound remains localized at the site of injection or diffuses and accumulates in distant organs. Animal experiments indicate that biopersistent nanomaterials taken up by monocyte-lineage cells in tissues, such as fluorescent alum surrogates, can first translocate to draining lymph nodes, and thereafter circulate in blood within phagocytes and reach the spleen, and, eventually, slowly accumulate in the brain.

http://www.ncbi.nlm.nih.gov/pubmed/22235051

"Animal experiments indicate that biopersistent nanomaterials taken up by monocyte-lineage cells in tissues, such as fluorescent alum surrogates, can first translocate to draining lymph nodes, and thereafter circulate in blood within phagocytes and reach the spleen, and, eventually, slowly accumulate in the brain"

From the World Journal of Pediatrics • May 2014

Aluminum exposure and toxicity in neonates: a practical guide to halt aluminum overload in the prenatal and perinatal periods

Fanni D1, Ambu R, Gerosa C, Nemolato S, Iacovidou N, Van Eyken P, Fanos V, Zaffanello M, Faa G.

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Abstract

BACKGROUND:

During the last years, human newborns have been overexposed to biologically reactive aluminum, with possible relevant consequences on their future health and on their susceptibility to a variety of diseases. Children, newborns and particularly preterm neonates are at an increased risk of aluminum toxicity because of their relative immaturity.

DATA SOURCES:

Based on recent original publications and classical data of the literatures, we reviewed the aluminum content in mother's food during the intrauterine life as well as in breast milk and infant formula during lactation. We also determined the possible role of aluminum in parenteral nutrition solutions, in adjuvants of vaccines and in pharmaceutical products. A special focus is placed on the relationship between aluminum overexposure and the insurgence of bone diseases.

RESULTS:

Practical points of management and prevention are suggested. Aluminum sources that infants may receive during the first 6 months of life are presented. In the context of prevention of possible adverse effects of aluminum overload in fetal tissues during development, simple suggestions to pregnant women are described. Finally, practical points of management and prevention are suggested.

CONCLUSIONS:

Pediatricians and neonatologists must be more concerned about aluminum content in all products our newborns are exposed to, starting from monitoring aluminum concentrations in milk- and soy-based formulas in which, on the basis of recent studies, there is still too much aluminum.

http://www.ncbi.nlm.nih.gov/pubmed/24801228

"Pediatricians and neonatologists must be more concerned about aluminum content in all products our newborns are exposed to"

> “We believe that macrophagic myofasciitis represents a localized histological hallmark of previous immunization with the aluminum hydroxide adjuvants contained in vaccines, rather than a primary or distinct inflammatory muscle disease”

From the Journal Child Neurology • June 2008

Macrophagic myofasciitis in children is a localized reaction to vaccination

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Abstract

Macrophagic myofasciitis is a novel, “inflammatory myopathy” described after a variety of vaccinations, almost exclusively in adults. We examined the relevance of histological findings of this myopathy to the clinical presentation in pediatric patients. Muscle biopsies from 8 children (7 months to 6 years old) with histological features of macrophagic myofasciitis were reviewed and correlated with the clinical manifestations. Patients underwent quadriceps muscle biopsy for suspected mitochondrial disease (4 patients), spinal muscular atrophy (2 patients), myoglobinuria (1 patient), and hypotonia with motor delay (1 patient). All biopsies showed identical granulomas composed of periodic acid-Schiff-positive and CD68-positive macrophages. Characteristic aluminum hydroxide crystals were identified by electron microscopy in 2 cases. The biopsy established diagnoses other than macrophagic myofasciitis in 5 patients: spinal muscular atrophy (2), Duchenne muscular dystrophy (1), phospho-glycerate kinase deficiency (1), and cytochrome c oxidase deficiency (1). Three children with manifestations and/or a family history of mitochondrial disease had otherwise morphologically normal muscle. All children had routine vaccinations between 2 months and 1 year before the biopsy, with up to 11 intramuscular injections, including the biopsy sites. There was no correlation between histological findings of macrophagic myofasciitis in biopsies and the clinical symptoms. We believe that macrophagic myofasciitis represents a localized histological hallmark of previous immunization with the aluminum hydroxide adjuvants contained in vaccines, rather than a primary or distinct inflammatory muscle disease.

http://www.ncbi.nlm.nih.gov/pubmed/18281624

“We conclude that the MMF lesion is secondary to intramuscular injection of aluminium hydroxide-containing vaccines”

From the Journal Brain • September 2001

Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle

Gherardi RK, Coquet M, Cherin P, Belec L, Moretto P, Dreyfus PA, Pellissier JF, Chariot P, Authier FJ.

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Abstract

Macrophagic myofasciitis (MMF) is an emerging condition of unknown cause, detected in patients with diffuse arthromyalgias and fatigue, and characterized by muscle infiltration by granular periodic acid-Schiff's reagent-positive macrophages and lymphocytes. Intracytoplasmic inclusions have been observed in macrophages of some patients. To assess their significance, electron microscopy was performed in 40 consecutive cases and chemical analysis was done by microanalysis and atomic absorption spectrometry. Inclusions were constantly detected and corresponded to aluminium hydroxide, an immunostimulatory compound frequently used as a vaccine adjuvant. A lymphocytic component was constantly observed in MMF lesions. Serological tests were compatible with exposure to aluminium hydroxide-containing vaccines. History analysis revealed that 50 out of 50 patients had received vaccines against hepatitis B virus (86%), hepatitis A virus (19%) or tetanus toxoid (58%), 3-96 months (median 36 months) before biopsy. Diffuse myalgias were more frequent in patients with than without an MMF lesion at deltoid muscle biopsy ($P < 0.0001$). Myalgia onset was subsequent to the vaccination (median 11 months) in 94% of patients. MMF lesion was experimentally reproduced in rats. We conclude that the MMF lesion is secondary to intramuscular injection of aluminium hydroxide-containing vaccines, shows both long-term persistence of aluminium hydroxide and an ongoing local immune reaction, and is detected in patients with systemic symptoms which appeared subsequently to vaccination.

http://www.ncbi.nlm.nih.gov/pubmed/11522584

From the Journal Brain • September 2001

Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle

Gherardi RK, Coquet M, Cherin P, Belec L, Moretto P, Dreyfus PA, Pellissier JF, Chariot P, Authier FJ.

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Abstract

Macrophagic myofasciitis (MMF) is an emerging condition of unknown cause, detected in patients with diffuse arthromyalgias and fatigue, and characterized by muscle infiltration by granular periodic acid-Schiff's reagent-positive macrophages and lymphocytes. Intracytoplasmic inclusions have been observed in macrophages of some patients. To assess their significance, electron microscopy was performed in 40 consecutive cases and chemical analysis was done by microanalysis and atomic absorption spectrometry. Inclusions were constantly detected and corresponded to aluminium hydroxide, an immunostimulatory compound frequently used as a vaccine adjuvant. A lymphocytic component was constantly observed in MMF lesions. Serological tests were compatible with exposure to aluminium hydroxide-containing vaccines. History analysis revealed that 50 out of 50 patients had received vaccines against hepatitis B virus (86%), hepatitis A virus (19%) or tetanus toxoid (58%), 3-96 months (median 36 months) before biopsy. Diffuse myalgias were more frequent in patients with than without an MMF lesion at deltoid muscle biopsy ($P < 0.0001$). Myalgia onset was subsequent to the vaccination (median 11 months) in 94% of patients. MMF lesion was experimentally reproduced in rats. We conclude that the MMF lesion is secondary to intramuscular injection of aluminium hydroxide-containing vaccines, shows both long-term persistence of aluminium hydroxide and an ongoing local immune reaction, and is detected in patients with systemic symptoms which appeared subsequently to vaccination.

http://www.ncbi.nlm.nih.gov/pubmed/11522584

"Inclusions were constantly detected and corresponded to aluminium hydroxide, an immunostimulatory compound frequently used as a vaccine adjuvant. Serological tests were compatible with exposure to aluminium hydroxide-containing vaccines"

From the Journal Alzheimers Disease • November 2005

Synergistic effects of iron and aluminum on stress-related gene expression in primary human neural cells

Alexandrov PN1, Zhao Y, Pogue AI, Tarr MA, Kruck TP, Percy ME, Cui JG, Lukiw WJ.

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Abstract

Disturbances in metal-ion transport, homeostasis, overload and metal ion-mediated catalysis are implicated in neuro-degenerative conditions such as Alzheimer's disease (AD). The mechanisms of metal-ion induced disruption of genetic function, termed genotoxicity, are not well understood. In these experiments we examined the effects of non-apoptotic concentrations of magnesium-, iron- and aluminum-sulfate on gene expression patterns in untransformed human neural (HN) cells in primary culture using high density DNA array profiling and Western immunoassay. Two week old HN cells were exposed to low micromolar magnesium, iron, or aluminum for 7 days, representing trace metal exposure over one-third of their lifespan. While total RNA yield and abundance were not significantly altered, both iron and aluminum were found to induce HSP27, COX-2, betaAPP and DAXX gene expression. Similarly up-regulated gene expression for these stress-sensing, pro-inflammatory and pro-apoptotic elements have been observed in AD brain. The combination of iron and aluminum together was found to be particularly effective in up-regulating these genes, and was preceded by the evolution of reactive oxygen intermediates as measured by 2',7'-dichlorofluorescein diacetate assay. These data indicate that physiologically relevant amounts of iron and aluminum are capable of inducing Fenton chemistry-triggered gene expression programs that may support downstream pathogenic responses and brain cell dysfunction.

http://www.ncbi.nlm.nih.gov/pubmed/16308480

"These data indicate that physiologically relevant [the normal amounts one might expect to find] amounts of iron and aluminum are capable of inducing Fenton chemistry-triggered gene expression programs that may support downstream pathogenic responses and brain cell dysfunction"

“Al-gel elicited vascular permeability increasing effects and toxic effects to macrophages”

From the Journal Vaccine • 1993

Studies on the toxicities of aluminium hydroxide and calcium phosphate as immunological adjuvants for vaccines

Goto N, Kato H, Maeyama J, Eto K, Yoshihara S.

Department of Safety Research on Biologics, National Institute of Health, Tokyo, Japan

Abstract

Aluminium hydroxide (Al) and calcium phosphate (Ca) have been used for many years as immunological adjuvants for biologicals. We investigated the toxic effects of both adjuvants with different physical properties. Al-gel elicited vascular permeability-increasing and toxic effects to macrophages (M phi), while its haemolytic effect was weak. Ca-gel elicited a significantly stronger haemolytic effect, but no other toxic effect. Incubation of M phi or polymorphonuclear leucocytes with Al-suspension resulted in the largest release of lactate dehydrogenase. Ca-suspension caused haemolysis of about 50% of that caused by Ca-gel.

http://www.ncbi.nlm.nih.gov/pubmed/8212836

From the Journal Biotechnic & Histochemistry • February 2015

A histological study of toxic effects of aluminium sulfate on rat hippocampus

Çabu N, Ouz EO, Tufan AÇ, Adıgüzel E.

Department of Histology and Embryology, Faculty of Medicine, Hacettepe University, Sihhiye Ankara, Turkey

Abstract

Aluminium has toxic effects on many organ systems of the human body. Aluminium toxicity also is a factor in many neurodegenerative diseases. We investigated changes in numbers of hippocampal neurons in rats exposed to aluminium using an optical fractionator and we investigated aluminium-induced apoptosis using the transferase mediated dUTP nick end labeling (TUNEL) assay. Twenty-four female rats were divided equally into control, sham and aluminium-exposed groups. The control group received no treatment. The two treatment groups were injected intraperitoneally with 1 ml 0.9% saline without (sham) and with 3 mg/ml aluminium sulfate every day for two weeks. Following the treatments, the brains were removed, the left hemisphere was used for hippocampal neuron counting using an optical fractionator and the right hemisphere was investigated using hippocampal TUNEL assay to determine the apoptotic index. The number of neurons in the stratum pyramidale of the hippocampus was significantly less in the aluminium group than in the control and sham groups; there was no significant difference between the control and sham groups. The apoptotic index also was significantly higher in the aluminium group than in the other two groups. We quantified the toxic effects of aluminium on the rat hippocampus and determined that apoptosis was the mechanism of aluminium-induced neuron death in the hippocampus.

http://www.ncbi.nlm.nih.gov/pubmed/25314162

“The apoptotic index also was significantly higher in the aluminium group than in the other two groups. We quantified the toxic effects of aluminium on the rat hippocampus and determined that apoptosis was the mechanism of aluminium-induced neuron death in the hippocampus”

From the Journal Critical Reviews In Toxicology • October 2014

Systematic review of potential health risks posed by pharmaceutical, occupational and consumer exposures to metallic and nanoscale aluminum, aluminum oxides, aluminum hydroxide and its soluble salts

Willhite CC, Karyakina NA, Yokel RA, Yenugadhati N, Wisniewski TM, Arnold IM, Momoli F, Krewski D.

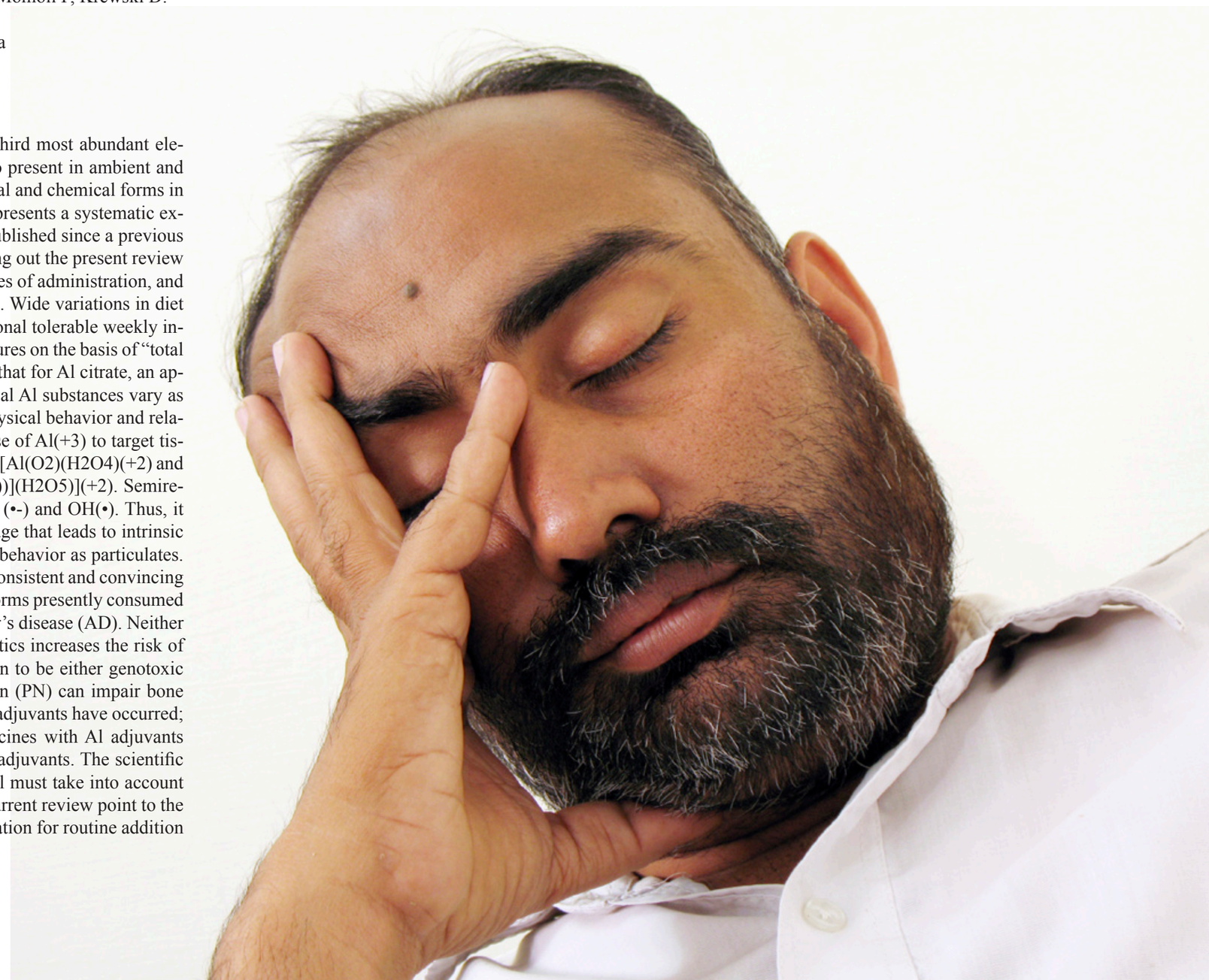
Risk Sciences International , Ottawa, ON , Canada

Abstract

Abstract Aluminum (Al) is a ubiquitous substance encountered both naturally (as the third most abundant element) and intentionally (used in water, foods, pharmaceuticals, and vaccines); it is also present in ambient and occupational airborne particulates. Existing data underscore the importance of Al physical and chemical forms in relation to its uptake, accumulation, and systemic bioavailability. The present review represents a systematic examination of the peer-reviewed literature on the adverse health effects of Al materials published since a previous critical evaluation compiled by Krewski et al. (2007) . Challenges encountered in carrying out the present review reflected the experimental use of different physical and chemical Al forms, different routes of administration, and different target organs in relation to the magnitude, frequency, and duration of exposure. Wide variations in diet can result in Al intakes that are often higher than the World Health Organization provisional tolerable weekly intake (PTWI), which is based on studies with Al citrate. Comparing daily dietary Al exposures on the basis of "total Al" assumes that gastrointestinal bioavailability for all dietary Al forms is equivalent to that for Al citrate, an approach that requires validation. Current occupational exposure limits (OELs) for identical Al substances vary as much as 15-fold. The toxicity of different Al forms depends in large measure on their physical behavior and relative solubility in water. The toxicity of soluble Al forms depends upon the delivered dose of Al(+3) to target tissues. Trivalent Al reacts with water to produce bidentate superoxide coordination spheres [Al(O2)(H2O4)(+2) and Al(H2O)6 (+3)] that after complexation with O2(•-), generate Al superoxides [Al(O2(•))](H2O5)](+2). Semireduced AlO2(•) radicals deplete mitochondrial Fe and promote generation of H2O2, O2 (•-) and OH(•). Thus, it is the Al(+3)-induced formation of oxygen radicals that accounts for the oxidative damage that leads to intrinsic apoptosis. In contrast, the toxicity of the insoluble Al oxides depends primarily on their behavior as particulates. Aluminum has been held responsible for human morbidity and mortality, but there is no consistent and convincing evidence to associate the Al found in food and drinking water at the doses and chemical forms presently consumed by people living in North America and Western Europe with increased risk for Alzheimer's disease (AD). Neither is there clear evidence to show use of Al-containing underarm antiperspirants or cosmetics increases the risk of AD or breast cancer. Metallic Al, its oxides, and common Al salts have not been shown to be either genotoxic or carcinogenic. Aluminum exposures during neonatal and pediatric parenteral nutrition (PN) can impair bone mineralization and delay neurological development. Adverse effects to vaccines with Al adjuvants have occurred; however, recent controlled trials found that the immunologic response to certain vaccines with Al adjuvants was no greater, and in some cases less than, that after identical vaccination without Al adjuvants. The scientific literature on the adverse health effects of Al is extensive. Health risk assessments for Al must take into account individual co-factors (e.g., age, renal function, diet, gastric pH). Conclusions from the current review point to the need for refinement of the PTWI, reduction of Al contamination in PN solutions, justification for routine addition of Al to vaccines, and harmonization of OELs for Al substances.

http://www.ncbi.nlm.nih.gov/pubmed/25233067

"The scientific literature on the adverse health effects of Al is extensive"



From the Journal Environmental Sciences and Pollution Research International
November 2014

Effects of aluminium and bacterial lipopolysaccharide on oxidative stress and immune parameters in roach, Rutilus rutilus L.

Jolly S, Jaffal A, Delahaut L, Palluel O, Porcher JM, Geffard A, Sanchez W, Betoulle S.

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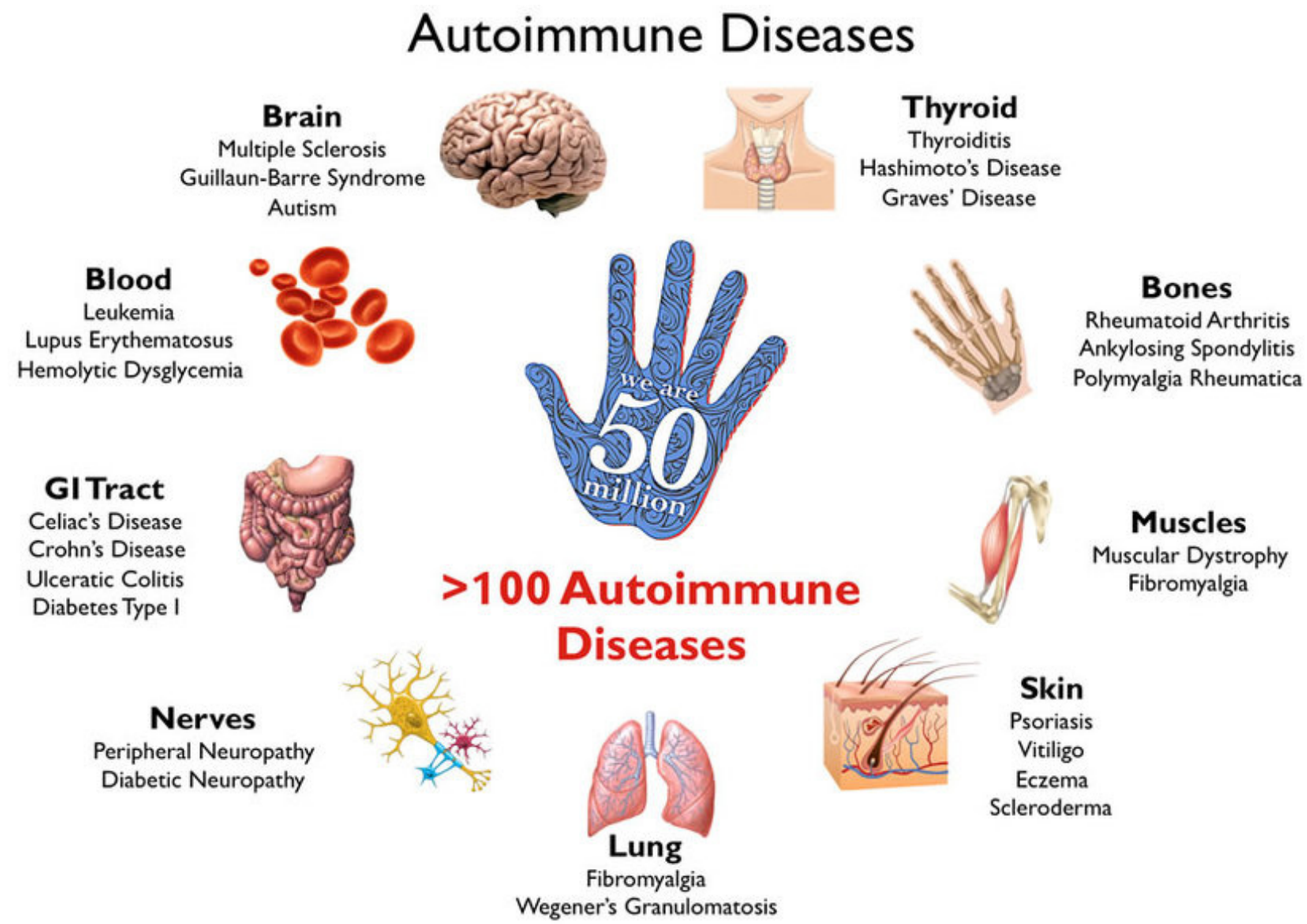
Abstract

Aluminium is used in diverse anthropogenic processes at the origin of pollution events in aquatic ecosystems. In the Champagne region (France), high concentrations of aluminium (Al) are detected due to vine-growing practices. In fish, little is known about the possible immune-related effects at relevant environmental concentrations. The present study analyzes the simultaneous effects of aluminium and bacterial lipopolysaccharide (LPS), alone and in combination, on toxicological biomarkers in the freshwater fish species Rutilus rutilus. For this purpose, roach treated or not with LPS were exposed to environmental concentrations of aluminium (100 µg/L) under laboratory-controlled conditions for 2, 7, 14 and 21 days. After each exposure time, we assessed hepatic lipoperoxidation, catalase activity, glutathione reductase activity and total glutathione content. We also analyzed cellular components related to the LPS-induced inflammatory response in possible target tissues, i.e. head kidney and spleen. Our results revealed a significant prooxidant effect in the liver cells and head kidney leukocytes of roach exposed to 100 µg of Al/L for 2 days. In liver, we observed more lipoperoxidation products and lower endogenous antioxidant activity levels such as glutathione reductase activity and total glutathione content. These prooxidant effects were associated with a higher oxidative burst in head kidney leukocytes, and they were all the more important in fish stimulated by LPS injection. These findings demonstrate that environmental concentrations of Al induce oxidative and immunotoxic effects in fish and are associated to an immunomodulatory process related to the inflammatory response.

http://www.ncbi.nlm.nih.gov/pubmed/24996940



> "These findings demonstrate that environmental concentrations of Al induce oxidative and immunotoxic effects in fish and are associated to an immunomodulatory process related to the inflammatory response"

Mucosal Immunology • May 2014

Aluminum enhances inflammation and decreases mucosal healing in experimental colitis in mice

Pineton de Chambrun G1, Body-Malapel M2, Frey-Wagner I3, Djouina M2, Deknuydt F4, Atrott K3, Esquerre N2, Altare F4, Neut C5, Arrieta MC6, Kanneganti TD7, Rogler G3, Colombel JF1, Cortot A1, Desreumaux P1, Vignal C2.

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6. Finlay Lab, Michael Smith Laboratories, University of British Columbia, Vancouver, British Columbia, Canada.
7. Department of Immunology, St Jude Children's Research Hospital, Memphis, Tennessee, USA.

Abstract

The increasing incidence of inflammatory bowel diseases (IBDs) in developing countries has highlighted the critical role of environmental pollutants as causative factors in their pathophysiology. Despite its ubiquity and immune toxicity, the impact of aluminum in the gut is not known. This study aimed to evaluate the effects of environmentally relevant intoxication with aluminum in murine models of colitis and to explore the underlying mechanisms. Oral administration of aluminum worsened intestinal inflammation in mice with 2,4,6-trinitrobenzene sulfonic acid- and dextran sodium sulfate-induced colitis and chronic colitis in interleukin 10-negative (IL10(-/-)) mice. Aluminum increased the intensity and duration of macroscopic and histologic inflammation, colonic myeloperoxidase activity, inflammatory cytokines expression, and decreased the epithelial cell renewal compared with control animals. Under basal conditions, aluminum impaired intestinal barrier function. In vitro, aluminum induced granuloma formation and synergized with lipopolysaccharide to stimulate inflammatory cytokines expression by epithelial cells. Deleterious effects of aluminum on intestinal inflammation and mucosal repair strongly suggest that aluminum might be an environmental IBD risk factor.

http://www.ncbi.nlm.nih.gov/pubmed/24129165

"Together, these results suggest for the first time that endothelial cells that line the cerebral vasculature may have biochemical attributes conducive to binding and targeting aluminum to selective anatomical regions of the brain, such as the hippocampus, with potential downstream pro-inflammatory and pathogenic consequences"

From the Journal Inorganic Biochemistry • September 2013

Selective accumulation of aluminum in cerebral arteries in Alzheimer's disease

Bhattacharjee S, Zhao Y, Hill JM, Culicchia F, Kruck TP, Percy ME, Pogue AI, Walton JR, Lukiw WJ.

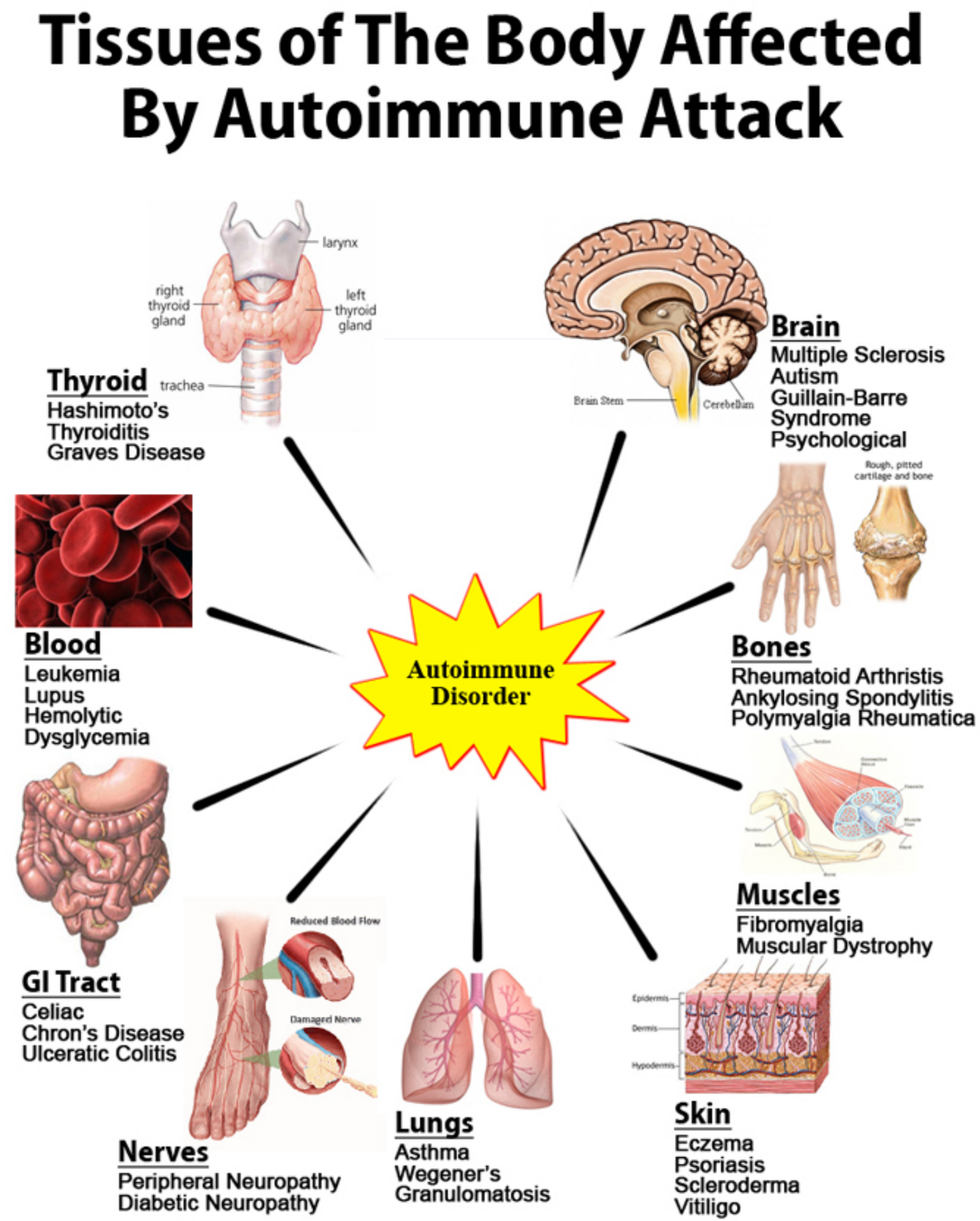
Neuroscience Center, Louisiana State University Health Sciences Center, New Orleans, LA 70112, USA

Abstract

Once biologically available aluminum bypasses gastrointestinal and blood-brain barriers, this environmentally-abundant neurotoxin has an exceedingly high affinity for the large pyramidal neurons of the human brain hippocampus. This same anatomical region of the brain is also targeted by the earliest evidence of Alzheimer's disease (AD) neuropathology. The mechanism for the selective targeting and transport of aluminum into the hippocampus of the human brain is not well understood. In an effort to improve our understanding of a pathological aluminum entry system into the brain, this study examined the aluminum content of 8 arteries that supply blood to the hippocampus, including the aorta and several cerebral arteries. In contrast to age-matched controls, in AD patients we found a gradient of increasing aluminum concentration from the aorta to the posterior cerebral artery that supplies blood to the hippocampus. Primary cultures of human brain endothelial cells were found to have an extremely high affinity for aluminum when compared to other types of brain cells. Together, these results suggest for the first time that endothelial cells that line the cerebral vasculature may have biochemical attributes conducive to binding and targeting aluminum to selective anatomical regions of the brain, such as the hippocampus, with potential downstream pro-inflammatory and pathogenic consequences.

http://www.ncbi.nlm.nih.gov/pubmed/23764827

"this environmentally-abundant neurotoxin has an exceedingly high affinity for the ... human brain"



From the Journal Environmental Health and Preventive Medicine • January 2011

Gene expression in primary cultured astrocytes affected by aluminum: alteration of chaperons involved in protein folding

Aremu DA, Ezomo OF, Meshitsuka S.

Division of Integrative Bioscience, Institute for Regenerative Medicine and Bio-function,
Graduate School of Medical Science, Tottori University, Yonago, Tottori, 683-8503, Japan.

Abstract

OBJECTIVES:
Aluminum is notorious as a neurotoxic metal. The aim of our study was to determine whether endoplasmic reticulum (ER) stress is involved in aluminum-induced apoptosis in astrocytes.

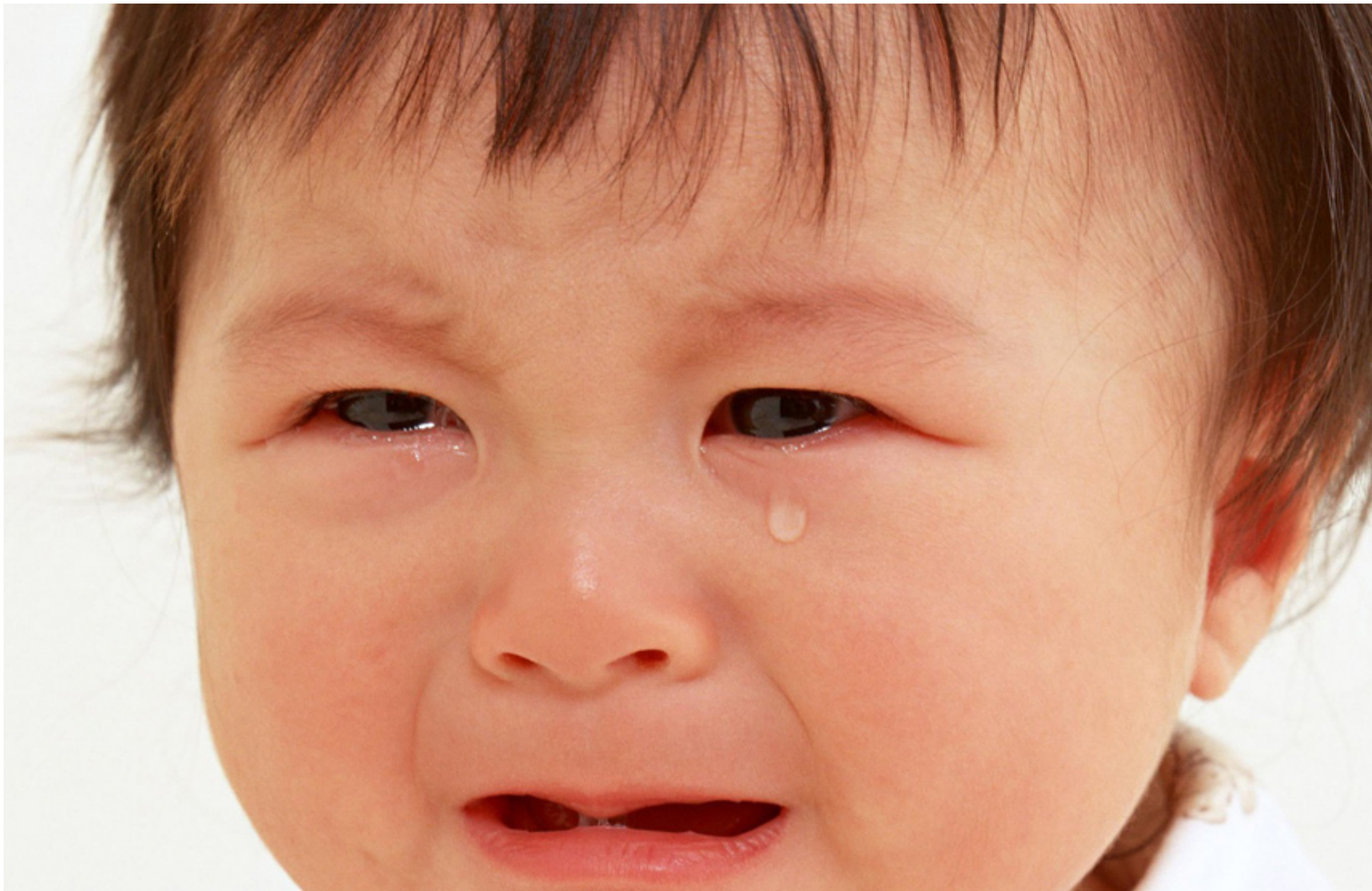
METHODS:
Mitochondrial RNA (mRNA) was analyzed by reverse transcription (RT)-PCR following pulse exposure of aluminum glycinate to primary cultured astrocytes. Tunicamycin was used as a positive control.

RESULTS:
Gene expression analysis revealed that Ire1 was up-regulated in astrocytes exposed to aluminum while Ire1 was up-regulated by tunicamycin. Exposure to aluminum glycinate, in contrast to tunicamycin, seemed to down-regulate mRNA expression of many genes, including the ER resident molecular chaperone BiP/Grp78 and Ca(2+)-binding chaperones (calnexin and calreticulin), as well as stanniocalcin 2 and OASIS. The down-regulation or non-activation of the molecular chaperons, whose expressions are known to be protective by increasing protein folding, may spell doom for the adaptive response. Exposure to aluminum did not have any significant effects on the expression of Bax and Bcl2 in astrocytes.

CONCLUSIONS:
The results of this study demonstrate that aluminum may induce apoptosis in astrocytes via ER stress by impairing the protein-folding machinery.

http://www.ncbi.nlm.nih.gov/pubmed/21432213

“The results of this study demonstrate that aluminum may induce apoptosis in astrocytes via ER stress by impairing the protein-folding machinery”



From the Journal Experimental Gerontology • April 2008

Effects of aluminium sulphate in the mouse liver: similarities to the aging process

Stacchiotti A, Lavazza A, Ferroni M, Sberveglieri G, Bianchi R, Rezzani R, Rodella LF.

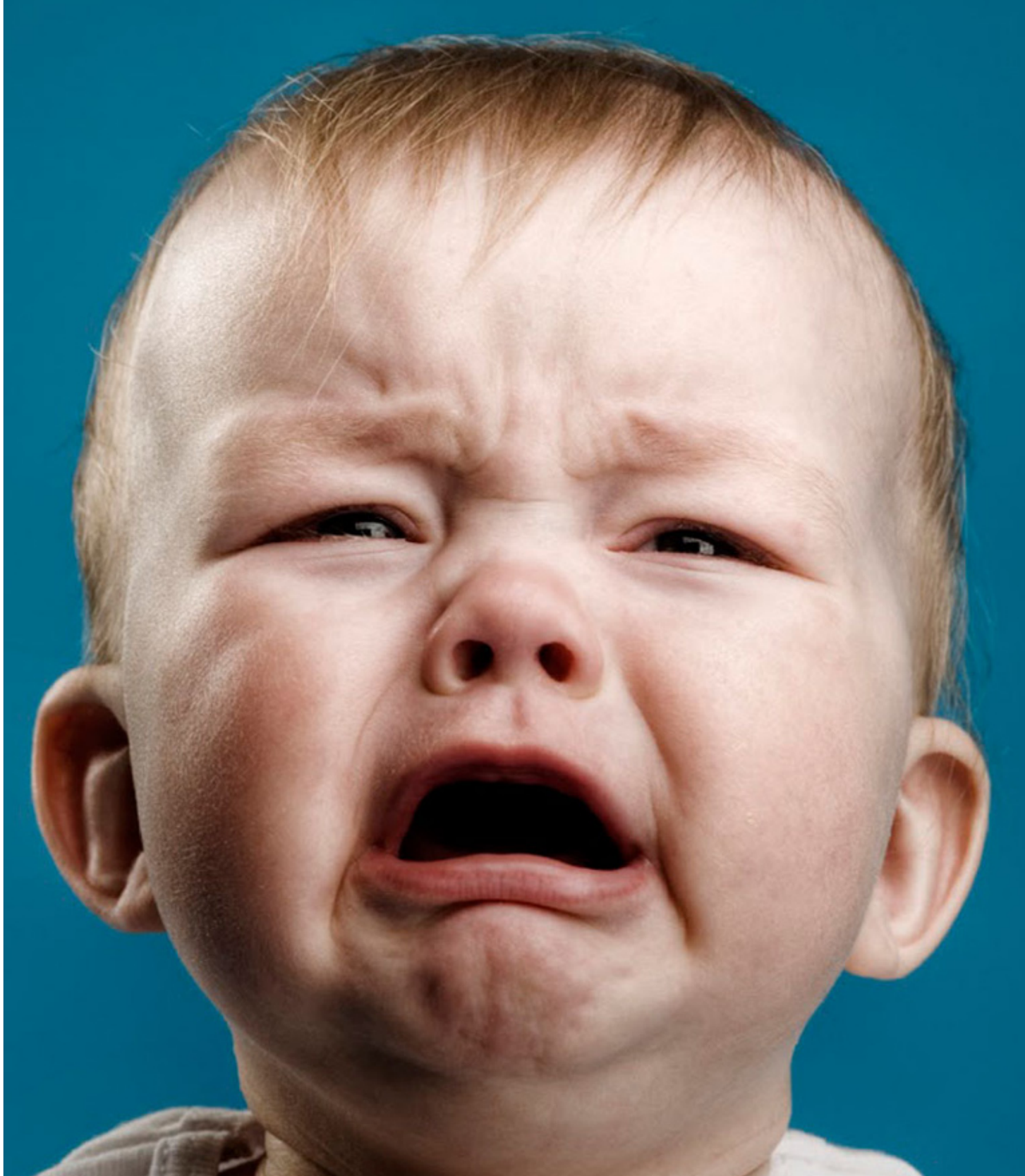
Department of Biomedical Sciences and Biotechnologies,
Brescia University, Brescia, Italy
stacchio@med.unibs.it

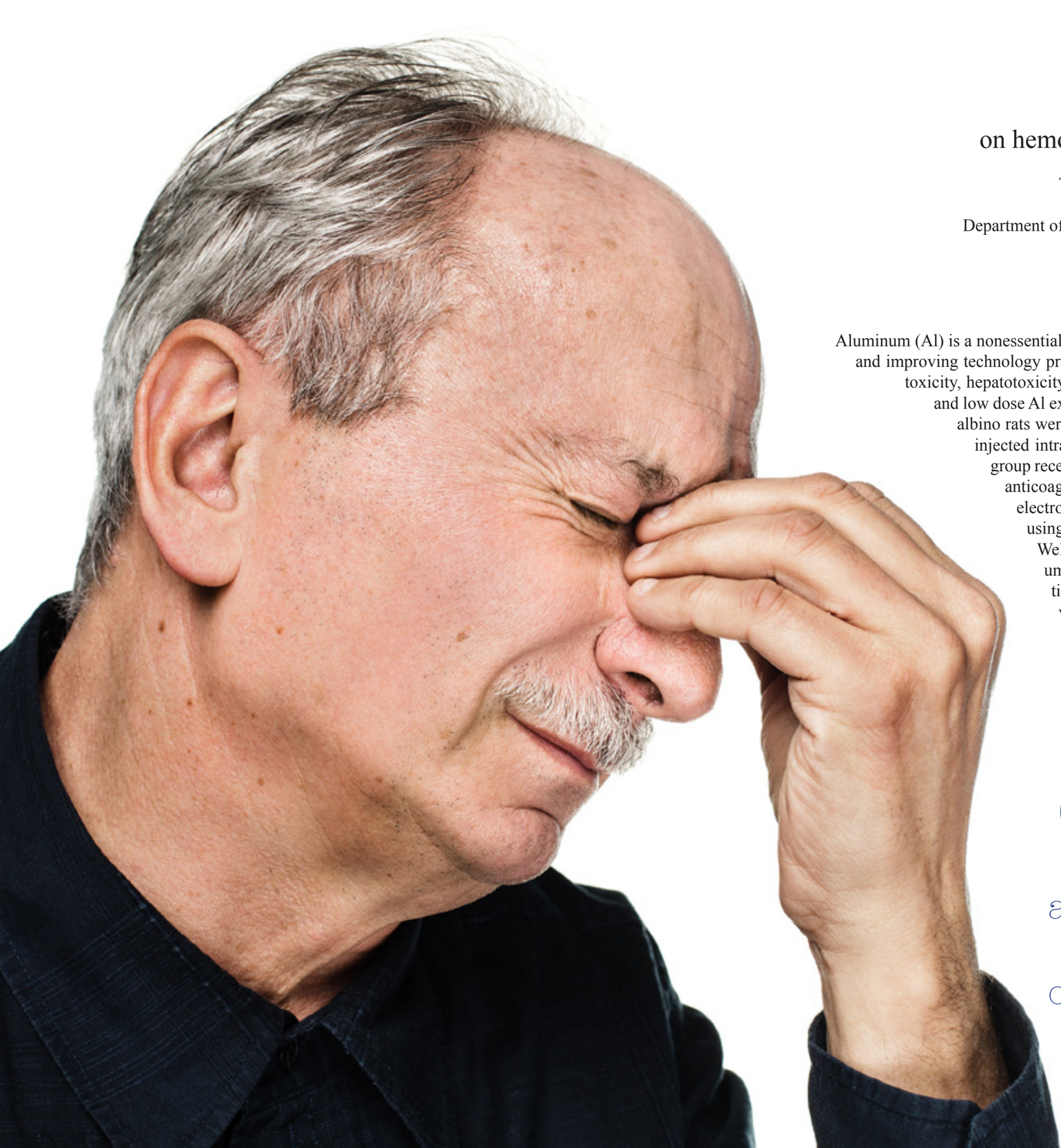
Abstract

Aluminium (Al) is a ubiquitous metal that is potentially toxic to the brain. Its effects on other fundamental organs are not completely understood. This morphological in vivo study sought to compare sublethal hepatotoxic changes and Al deposition in adult mice that orally ingested Al sulphate daily for 10 months, in age matched control mice that drank tap water and in senescent mice (24 months old). Livers were examined for collagen deposition using Sirius red and Masson, for iron accumulation using Perls' stain. Light, electron microscopy and morphometry were used to assess fibrosis and vascular changes. Scanning transmission electron microscopy and EDX microanalysis were used to detect in situ elemental Al. Iron deposition, transferrin receptor expression were significantly altered following Al exposure and in the aged liver but were unaffected in age matched control mice. In Al treated mice as in senescent mice, endothelial thickness was increased and porosity was decreased like perisinusoidal actin. Furthermore, Al stimulated the deposition of collagen and laminin, mainly in acinar zones 1 and 3. Pseudocapillarization and periportal laminin in senescent mice were similar to Al treated adult liver. In conclusion, prolonged Al sulphate intake accelerates features of senescence in the adult mice liver.

http://www.ncbi.nlm.nih.gov/pubmed/18337038

> "In conclusion, prolonged Al sulphate intake accelerates features of senescence [aging] in the adult mice liver"





From the Journal Archives Of Toxicology • January 2007

The effects of low dose aluminum on hemorheological and hematological parameters in rats

Turgut S1, Bor-Kucukatay M, Emmungil G, Atsak P, Turgut G.

Department of Physiology, Medical Faculty, Pamukkale University, 20020 Denizli, Turkey
sturgut@pamukkale.edu.tr

Abstract

Aluminum (Al) is a nonessential element and humans are constantly exposed to Al as a result of an increase in industrialization and improving technology practices. Al toxicity can induce several clinical disorders such as neurotoxicity, gastrointestinal toxicity, hepatotoxicity, bone diseases, and anemia. This study aimed at evaluating the possible effects of short term and low dose Al exposure on hemorheological and hematological parameters in rats. Fourteen young, male Wistar albino rats were divided into two groups: 1 mg/200 g body weight of aluminum sulfate (Al(2)(SO(4))(3) was injected intraperitoneally to the first group for two weeks, three times a week. The animals of the control group received only physiological saline solution during this period. At the end of the experimental period, anticoagulated blood samples were collected and hematological parameters were determined using an electronic hematology analyzer. Red blood cell (RBC) deformability and aggregation were measured using an ektacytometer (LORCA) and plasma and whole blood viscosities were determined with a Wells-Brookfield cone-plate rotational viscometer. Significant decreases in mean corpuscular volume (MCV), red blood cell (RBC) deformability at low shear stress levels, the aggregation half time (t1/2) and the amplitude (AMP) of aggregation and significant increments in whole blood viscosity (WBV) at native and 40% hematocrit (Hct) of Al-treated rats have been observed. In conclusion, low dose Al(2)(SO(4))(3) exposure for a short-time may be responsible for alterations in either rheological properties of blood or hemorheological properties through a remarkable effect on RBC membrane mechanical properties. These alterations may also play an important role in the development of anemia in the Al-treated animals.

http://www.ncbi.nlm.nih.gov/pubmed/16721596

> “These alterations may also play an important role in the development of anemia in the Al-treated animals”

From the Journal Neuroimmunology • July 2006

Aluminum and copper in drinking water enhance inflammatory or oxidative events specifically in the brain

Becaria A, Lahiri DK, Bondy SC, Chen D, Hamadeh A, Li H, Taylor R, Campbell A.

Department of Community and Environmental Medicine,
Center for Occupational and Environmental Health Sciences,
University of California, Irvine, Irvine, CA 92697-1825, USA

Abstract

Inflammatory and oxidative events are up-regulated in the brain of AD patients. It has been reported that in animal models of AD, exposure to aluminum (Al) or copper (Cu) enhanced oxidative events and accumulation of amyloid beta (Abeta) peptides. The present study was designed to evaluate the effect of a 3-month exposure of mice to copper sulfate (8 microM), aluminum lactate (10 or 100 microM), or a combination of the salts. Results suggest that although Al or Cu may independently initiate inflammatory or oxidative events, they may function cooperatively to increase APP levels.

http://www.ncbi.nlm.nih.gov/pubmed/16697052

> “Results suggest that although Al or Cu may independently initiate inflammatory or oxidative events, they may function cooperatively”

From the Journal Zhongguo Zhong Yao Za Zhi or the Chinese Journal of Medicine
December 1998

Influence of alum on intestinal flora in mice

Yan M1, Song H, Zhang L, Wang Y, Wu Y, Zhou Z.

Institute of Chinese Materia Medica,
China Academy of Traditional Chinese Medicine, Beijing 100700

Abstract

OBJECTIVE:
To observe the influence of alum on the intestinal microecological balance in normal microorganisms.

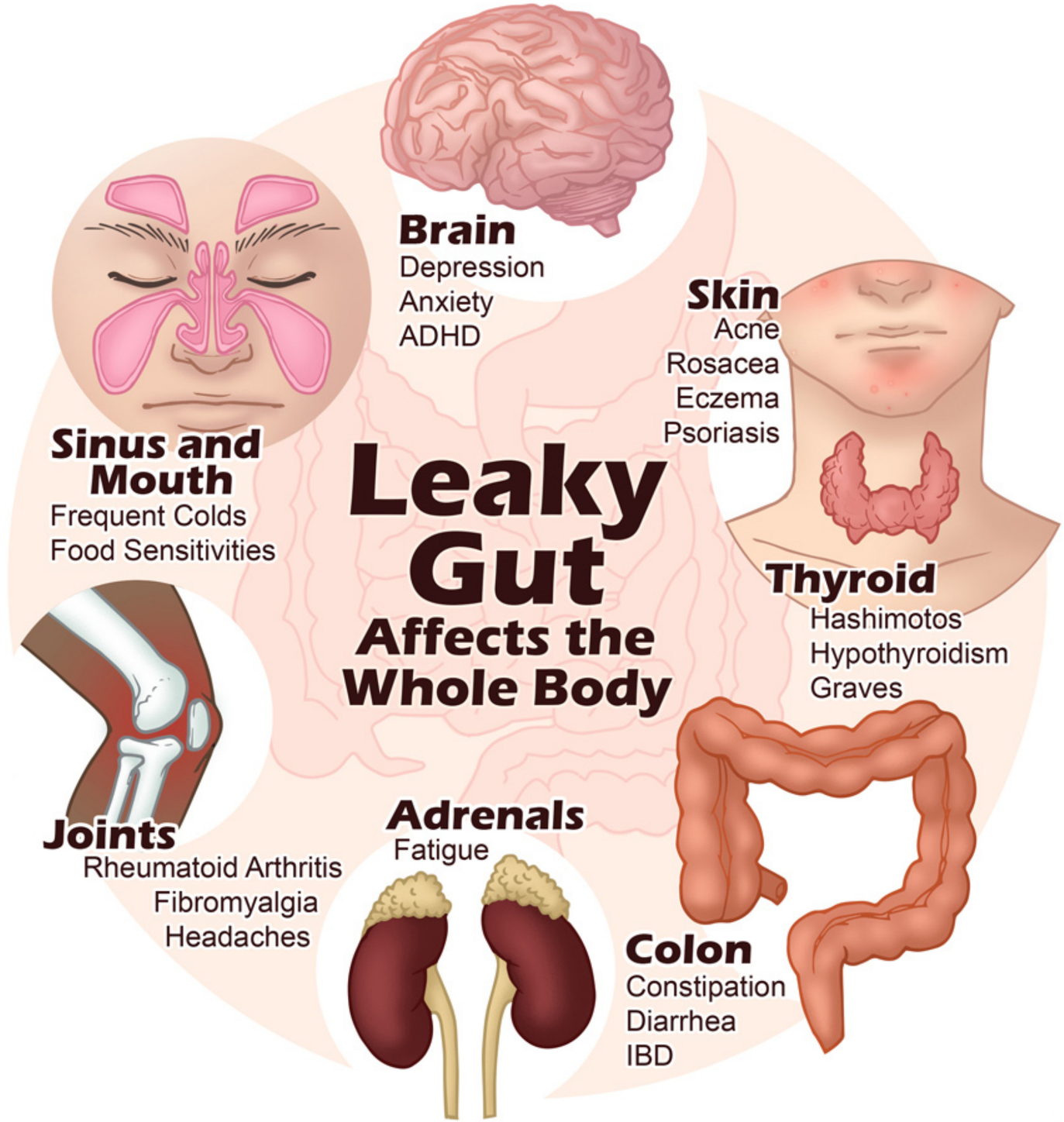
METHOD:
The mice were administered orally with alum of a small dosage(0.25/kg) and a large dosage(1 g/kg) for half a month, two months and three months, and a micro flora analysis of the mice was carried out at intervals of the above mentioned administrations.

RESULT:
The intestinal flora in the animals administered with alum was imbalanced. The counts of bifidobacteria and lactobacilli closely related to human physiological activities were decreased. The counts of pathogenic E. Coli significantly increased; and the longer the animals were treated with alum, the stronger the microecological balance was influenced.

CONCLUSION:
Alum could induce imbalance of the normal intestinal flora in mice.

http://www.ncbi.nlm.nih.gov/pubmed/12242827

> “Alum could induce imbalance of the normal intestinal flora in mice”



From the Journal Vaccine • October 1995

Adjuvants for human vaccines current status, problems and future prospects

Gupta RK, Siber GR.

Massachusetts Public Health Biologic Laboratories,
State Laboratory Institute, Boston 02130, USA

Abstract

Adjuvants help antigen to elicit an early, high and long-lasting immune response with less antigen, thus saving on vaccine production costs. In recent years, adjuvants received much attention because of the development of purified, subunit and synthetic vaccines which are poor immunogens and require adjuvants to evoke the immune response. With the use of adjuvants immune response can be selectively modulated to major histocompatibility complex (MHC) class I or MHC class II and Th1 or Th2 type, which is very important for protection against diseases caused by intracellular pathogens such as viruses, parasites and bacteria (Mycobacterium). A number of problems are encountered in the development and use of adjuvants for human vaccines. The biggest issue with the use of adjuvants for human vaccines, particularly routine childhood vaccines, is the toxicity and adverse side-effects of most of the adjuvant formulations. At present the choice of adjuvants for human vaccination reflects a compromise between a requirement for adjuvanticity and an acceptable low level of side-effects. Other problems with the development of adjuvants include restricted adjuvanticity of certain formulations to a few antigens, use of aluminum adjuvants as reference adjuvant preparations under suboptimal conditions, non-availability of reliable animal models, use of non-standard assays and biological differences between animal models and humans leading to the failure of promising formulations to show adjuvanticity in clinical trials. The most common adjuvants for human use today are still aluminum hydroxide and aluminum phosphate, although calcium phosphate and oil emulsions also have some use in human vaccinations. During the last 15 years much progress has been made on development, isolation and chemical synthesis of alternative adjuvants such as derivatives of muramyl dipeptide, monophosphoryl lipid A, liposomes, QS21, MF-59 and immunostimulating complexes (ISCOMS). Other areas in adjuvant research which have received much attention are the controlled release of vaccine antigens using biodegradable polymer microspheres and reciprocal enhanced immunogenicity of protein-polysaccharide conjugates. Biodegradable polymer microspheres are being evaluated for targeting antigens on mucosal surfaces and for controlled release of vaccines with an aim to reduce the number of doses required for primary immunization. Reciprocal enhanced immunogenicity of protein-polysaccharide conjugates will be useful for the development of combination vaccines.

http://www.ncbi.nlm.nih.gov/pubmed/8585280

“A number of problems are encountered in the development and use of adjuvants for human vaccines. The biggest issue with the use of adjuvants for human vaccines, particularly routine childhood vaccines, is the toxicity and adverse side-effects of most of the adjuvant formulations”

From the Journal Vaccine • 1993

Studies on the toxicities of aluminium hydroxide and calcium phosphate as immunological adjuvants for vaccines

Goto N, Kato H, Maeyama J, Eto K, Yoshihara S.

Department of Safety Research on Biologics, National Institute of Health, Tokyo, Japan

Abstract

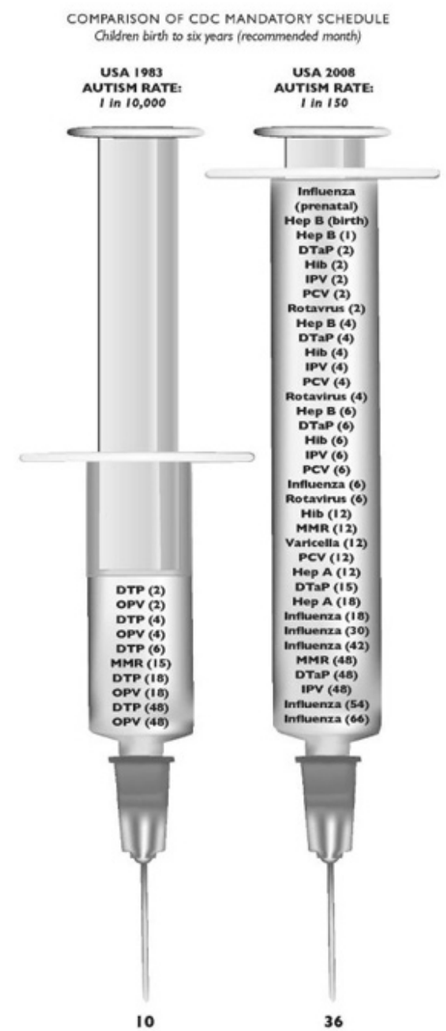
Aluminium hydroxide (Al) and calcium phosphate (Ca) have been used for many years as immunological adjuvants for biologicals. We investigated the toxic effects of both adjuvants with different physical properties. Al-gel elicited vascular permeability-increasing and toxic effects to macrophages (M phi), while its haemolytic effect was weak. Ca-gel elicited a significantly stronger haemolytic effect, but no other toxic effect. Incubation of M phi or polymorphonuclear leucocytes with Al-suspension resulted in the largest release of lactate dehydrogenase. Ca-suspension caused haemolysis of about 50% of that caused by Ca-gel.

http://www.ncbi.nlm.nih.gov/pubmed/8212836

> “Al-gel elicited vascular permeability-increasing and toxic effects to macrophages”

ARE WE POISONING OUR KIDS

IN THE NAME OF PROTECTING THEIR HEALTH?



Green our vaccines. And administer them with greater care.

Mercury. Aluminum. Formaldehyde. Ether. Antifreeze. Not exactly what you'd expect—or want—to find in your child's vaccinations. Vaccines that are supposed to safeguard their health yet, according to our studies, can also do harm to some children.

The statistics speak for themselves. Since 1983, the number of vaccines the CDC recommends we give to our kids has gone from 10 to 36, a whopping increase of 260%. And, with it, the prevalence of neurological disorders like autism and ADHD has grown exponentially as well.

Just a coincidence? We don't think so. Thousands of parents believe their child's regression into autism was triggered, if not caused, by over-immunization with toxic ingredients and live viruses found in vaccines. The Centers for Disease Control and the American Academy of Pediatrics dispute this but independent research and the first-hand accounts of parents tell a different story.

Why are we giving our children so many more vaccines so early in life?
Why do we only test vaccines individually and never consider the combination risk of vaccines administered together? Given the dramatic rise of autism to epidemic levels, isn't it time for the scientific community to seriously consider the anecdotal evidence of so many parents? We urge the CDC and AAP to help us find the answers to these questions and learn why the increase in the number and composition of so many vaccinations has led to a surge in neurodevelopmental disorders. Our children deserve no less.

GENERATION RESCUE
www.generationrescue.org

We want to thank Jim Carrey and Jenny McCarthy for their generous support of Generation Rescue and their neverending commitment to solving the growing challenges of autism.

Annali Dell' Istituto Superiore di Sanita • 1993

Behavioural effects of gestational exposure to aluminium

Rankin J, Sedowofia K, Clayton R, Manning A.

Institute of Cell, Animal and Population Biology, Edinburgh, UK

Abstract

The involvement of aluminium in the aetiology of a number of human pathological diseases has altered its status from being a nontoxic, nonabsorbable, harmless element. This maybe of particular concern to the developing foetus which is more susceptible to agents and at lower levels than the adult. Little attention has been given to aluminium's potential reproductive toxicity until recently and further research is required for a full evaluation of its toxicity. Our preliminary results demonstrate behavioural and neurochemical alterations in the offspring of mice exposed to aluminium during gestation. Further, the effects of such exposure are also present in the adult animal suggesting persistent changes in behaviour following prenatal exposure.

http://www.ncbi.nlm.nih.gov/pubmed/8129261

"... suggesting persistent changes in behaviour following prenatal exposure"

> The fluorescent nanodiamond technology is a choice methodology for studying distribution, persistence and long-term neurotoxicity of alum adjuvants

From the Journal BMC Medicine • June 2015

Fluorescent nanodiamonds as a relevant tag for the assessment of alum adjuvant particle biodisposition

Eidi H1,2, David MO3, Crépeaux G4, Henry L5, Joshi V6, Berger MH7, Sennour M8, Cadusseau J9,10, Gherardi RK11, Curmi PA12

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Abstract

BACKGROUND:

Aluminum oxyhydroxide (alum) is a crystalline compound widely used as an immunologic adjuvant of vaccines. Concerns linked to alum particles have emerged following recognition of their causative role in the so-called macrophagic myofasciitis (MMF) lesion in patients with myalgic encephalomyelitis, revealing an unexpectedly long-lasting biopersistence of alum within immune cells and a fundamental misconception of its biodisposition. Evidence that aluminum-coated particles phagocytozed in the injected muscle and its draining lymph nodes can disseminate within phagocytes throughout the body and slowly accumulate in the brain further suggested that alum safety should be evaluated in the long term. However, lack of specific staining makes difficult the assessment of low quantities of bona fide alum adjuvant particles in tissues.

METHODS:

We explored the feasibility of using fluorescent functionalized nanodiamonds (mfNDs) as a permanent label of alum (Alhydrogel(®)). mfNDs have a specific and perfectly photostable fluorescence based on the presence within the diamond lattice of nitrogen-vacancy centers (NV centers). As the NV center does not bleach, it allows the microspectrometric detection of mfNDs at very low levels and in the long-term. We thus developed fluorescent nanodiamonds functionalized by hyperbranched polyglycerol (mfNDs) allowing good coupling and stability of alum:mfNDs (AluDia) complexes. Specificities of AluDia complexes were comparable to the whole reference vaccine (anti-hepatitis B vaccine) in terms of particle size and zeta potential.

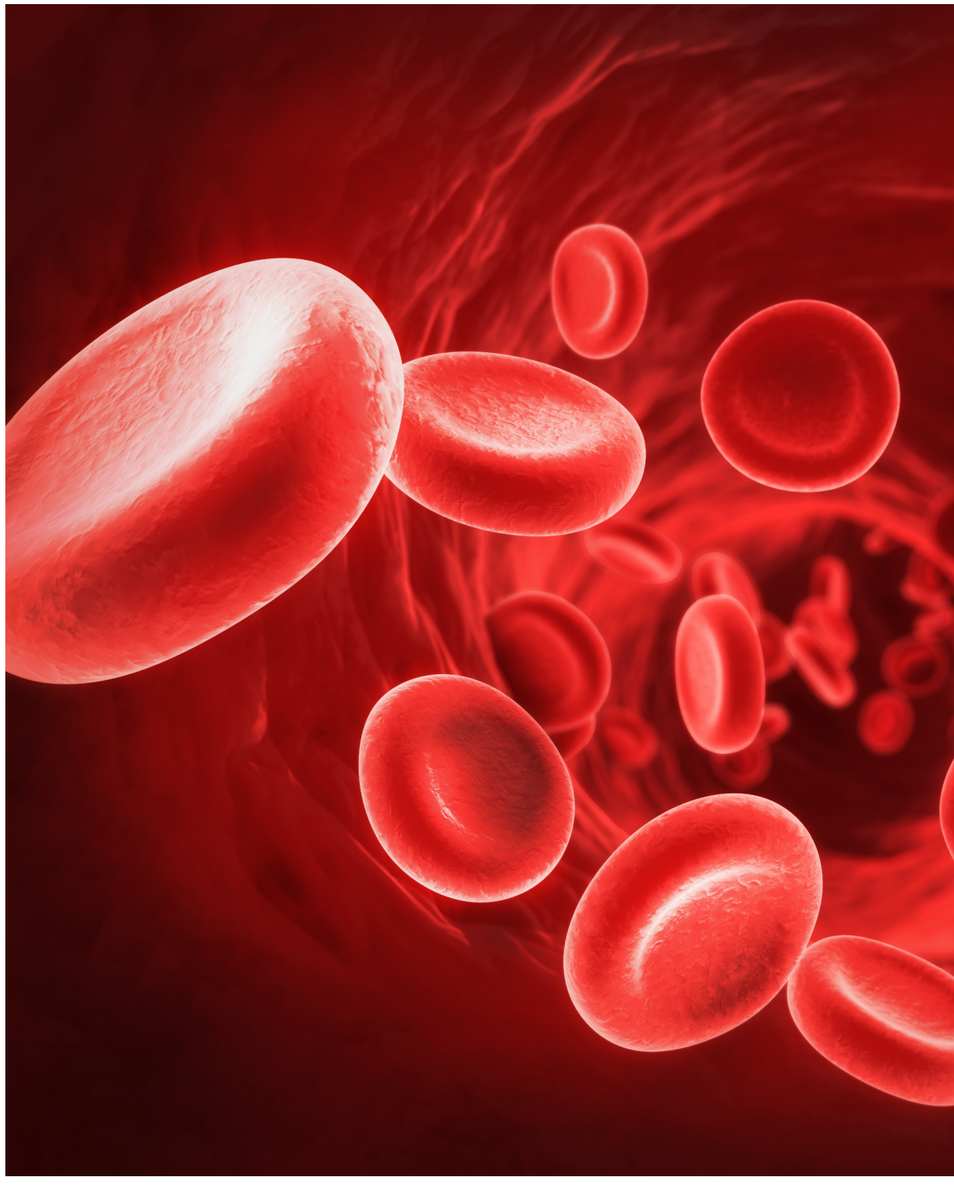
RESULTS:

In vivo, AluDia injection was followed by prompt phagocytosis and AluDia particles remained easily detectable by the specific signal of the fND particles in the injected muscle, draining lymph nodes, spleen, liver and brain. In vitro, mfNDs had low toxicity on THP-1 cells and AluDia showed cell toxicity similar to alum alone. Expectedly, AluDia elicited autophagy, and allowed highly specific detection of small amounts of alum in autophagosomes.

CONCLUSIONS:

The fluorescent nanodiamond technology is able to overcome the limitations of previously used organic fluorophores, thus appearing as a choice methodology for studying distribution, persistence and long-term neurotoxicity of alum adjuvants and beyond of other types of nanoparticles.

http://www.ncbi.nlm.nih.gov/pubmed/26082187



From the Journal Clinical and Experimental Immunology • January 2014

Effects of adjuvants for human use in systemic lupus erythematosus (SLE)-prone (New Zealand black/New Zealand white) F1 mice

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Abstract

The safety of four different adjuvants was assessed in lupus-prone New Zealand black/New Zealand white (BW)F1 mice. Four groups of mice were injected intraperitoneally with incomplete Freund's adjuvant (IFA), complete Freund's adjuvant (CFA), squalene (SQU) or aluminium hydroxide (ALU). An additional group received plain phosphate-buffered saline (PBS) (UNT group). Mice were primed at week 9 and boosted every other week up to week 15. Proteinuria became detectable at weeks 17 (IFA group), 24 (CFA group), 28 (SQU and ALU groups) and 32 (UNT group). Different mean values were obtained among the groups from weeks 17 to 21 [week 17: one-way analysis of variance (anova) $P = 0{\cdot}016$; weeks 18 and 19: $P = 0{\cdot}048$; weeks 20 and 21: $P = 0{\cdot}013$] being higher in the IFA group than the others [Tukey's honestly significant difference (HSD) post-test $P < 0{\cdot}05$]. No differences in anti-DNA antibody levels were observed among groups. Anti-RNP/Sm antibody developed at week 19 in only one CFA-treated mouse. Mean mouse weight at week 18 was lower in the ALU group than the IFA (Tukey's HSD post-test $P = 0{\cdot}04$), CFA ($P = 0{\cdot}01$) and SQU ($P < 0{\cdot}0001$) groups, while the mean weight in the SQU group was higher than in the IFA ($P = 0{\cdot}009$), CFA ($P = 0{\cdot}013$) and UNT ($P = 0{\cdot}005$) groups. The ALU group weight decreased by almost half between weeks 29 and 31, indicating some toxic effect of ALU in the late post-immunization period. Thus, SQU was the least toxic adjuvant as it did not (i) accelerate proteinuria onset compared to IFA; (ii) induce toxicity compared to ALU or (iii) elicit anti-RNP/Sm autoantibody, as occurred in the CFA group.

http://www.ncbi.nlm.nih.gov/pubmed/24112107

> "The ALU group weight decreased by almost half between weeks 29 and 31, indicating some toxic effect of ALU"

From the Journal Lupus • February 2012

Macrophagic myofasciitis: characterization and pathophysiology

Gherardi RK, Authier FJ.

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Abstract

Aluminium oxyhydroxide (alum), a nanocrystalline compound forming agglomerates, has been used in vaccines for its immunological adjuvant effect since 1927. Alum is the most commonly used adjuvant in human and veterinary vaccines, but the mechanisms by which it stimulates immune responses remain incompletely understood. Although generally well tolerated, alum may occasionally cause disabling health problems in presumably susceptible individuals. A small proportion of vaccinated people present with delayed onset of diffuse myalgia, chronic fatigue and cognitive dysfunction, and exhibit very long-term persistence of alum-loaded macrophages at the site of previous intramuscular (i.m.) immunization, forming a granulomatous lesion called macrophagic myofasciitis (MMF). Clinical symptoms associated with MMF are paradigmatic of the recently delineated 'autoimmune/inflammatory syndrome induced by adjuvants' (ASIA). The stereotyped cognitive dysfunction is reminiscent of cognitive deficits described in foundry workers exposed to inhaled Al particles. Alum safety concerns will largely depend on whether the compound remains localized at the site of injection or diffuses and accumulates in distant organs. Animal experiments indicate that biopersistent nanomaterials taken up by monocyte-lineage cells in tissues, such as fluorescent alum surrogates, can first translocate to draining lymph nodes, and thereafter circulate in blood within phagocytes and reach the spleen, and, eventually, slowly accumulate in the brain.

http://www.ncbi.nlm.nih.gov/pubmed/22235051

> "Animal experiments indicate that biopersistent nanomaterials ... such as fluorescent alum surrogates ... slowly accumulate in the brain"

From the Journal Immunology and Allergy Clinics of North America • November 2003

Aluminum inclusion macrophagic myofasciitis: a recently identified condition

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Abstract

The authors conclude that the persistence of aluminum hydroxide at the site of intramuscular injection is a novel finding which has an exact significance that remains to be established fully. It seems mandatory to evaluate possible long-term adverse effects induced by this compound, because this issue has not been addressed (in the past, aluminum hydroxide was believed to be cleared quickly from the body). If safety concerns about the long-term effects of aluminum hydroxide are confirmed, novel and alternative vaccine adjuvants to rescue vaccine-based strategies should be proposed to ensure the enormous benefit for public health that these vaccines provide worldwide.

http://www.ncbi.nlm.nih.gov/pubmed/14753387

> "in the past, aluminum hydroxide was believed to be cleared quickly from the body"

From the Journal Pharmacology & Toxicology • April 1992

Aluminium-adjuvanted vaccines transiently increase aluminium levels in murine [mouse] brain tissue

Redhead K, Quinlan GJ, Das RG, Gutteridge JM.

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Abstract

Aluminium is widely used as an adjuvant in human vaccines, and children can often receive up to 3.75 mg of parenteral aluminium during the first six months of life. We show that intraperitoneal injection of aluminium adsorbed vaccines into mice causes a transient rise in brain tissue aluminium levels peaking around the second and third day after injection. This rise is not seen in the saline control group of animals or with vaccine not containing aluminium. It is likely that aluminium is transported to the brain by the iron-binding protein transferrin and enters the brain via specific transferrin receptors.

http://www.ncbi.nlm.nih.gov/pubmed/1608913

“Aluminium is widely used as an adjuvant in human vaccines, and children can often receive up to 3.75 mg of parenteral aluminium during the first six months of life. We show that intraperitoneal injection of aluminium adsorbed vaccines into mice causes a transient rise in brain tissue aluminium levels peaking around the second and third day after injection”

From the Journal Frontiers in Neurology • February 2015

Biopersistence and brain translocation of aluminum adjuvants of vaccines

Gherardi RK, Eidi H, Crépeaux G, Authier FJ, Cadusseau J.

Faculté de Médecine and Faculté des Sciences et Technologie,
INSERM U955 Team 10, Université Paris Est-Créteil , Créteil , France

Abstract

Aluminum oxyhydroxide (alum) is a crystalline compound widely used as an immunological adjuvant of vaccines. Concerns linked to the use of alum particles emerged following recognition of their causative role in the so-called macrophagic myofasciitis (MMF) lesion detected in patients with myalgic encephalomyelitis/chronic fatigue/syndrome. MMF revealed an unexpectedly long-lasting biopersistence of alum within immune cells in presumably susceptible individuals, stressing the previous fundamental misconception of its biodisposition. We previously showed that poorly biodegradable aluminum-coated particles injected into muscle are promptly phagocytosed in muscle and the draining lymph nodes, and can disseminate within phagocytic cells throughout the body and slowly accumulate in brain. This strongly suggests that long-term adjuvant biopersistence within phagocytic cells is a prerequisite for slow brain translocation and delayed neurotoxicity. The understanding of basic mechanisms of particle biopersistence and brain translocation represents a major health challenge, since it could help to define susceptibility factors to develop chronic neurotoxic damage. Biopersistence of alum may be linked to its lysosome-destabilizing effect, which is likely due to direct crystal-induced rupture of phagolysosomal membranes. Macrophages that continuously perceive foreign particles in their cytosol will likely reiterate, with variable interindividual efficiency, a dedicated form of autophagy (xenophagy) until they dispose of alien materials. Successful compartmentalization of particles within double membrane autophagosomes and subsequent fusion with repaired and re-acidified lysosomes will expose alum to lysosomal acidic pH, the sole factor that can solubilize alum particles. Brain translocation of alum particles is linked to a Trojan horse mechanism previously described for infectious particles (HIV, HCV), that obeys to CCL2, signaling the major inflammatory monocyte chemoattractant.

http://www.ncbi.nlm.nih.gov/pubmed/25699008

> “This strongly suggests that long-term adjuvant biopersistence within phagocytic cells is a prerequisite for slow brain translocation and delayed neurotoxicity”

From the Journal
Bulletin de l'Academie Nationale de Medicine
January 2014

Biopersistence and systemic distribution of intramuscularly injected particles: what impact on long-term tolerability of alum adjuvants?

Gherardi RK, Cadusseau J, Authier FJ.

Abstract

Aluminium oxyhydroxide (alum), a nanocrystalline compound that forms agglomerates, has been widely used as a vaccine adjuvant since 1927, but the mechanisms by which it stimulates immune responses remain poorly understood. Although generally well tolerated, alum may occasionally cause chronic health problems in presumably susceptible individuals. Some individuals may rarely develop delayed-onset diffuse myalgia, chronic exhaustion and cognitive dysfunction, associated with long-term persistence (up to 12 years) of alum-loaded macrophages at site of i.m. immunization, defining so-called macrophagic myofasciitis (MMF). Symptoms are consistent with the chronic fatigue/myalgic encephalomyelitis (CFS/ME) syndrome, and have been used as a paradigm of the "autoimmune/inflammatory syndrome induced by adjuvants" (ASIA). Cognitive dysfunction is reminiscent of that described in workers exposed to inhaled Al particles. Individual susceptibility may influence both alum biopersistence and difusion away from injection sites. Biopersistent particles such as fluorescent alum-coated nanohybrids, when injected into mouse muscle, are captured by monocyte-lineage cells and then carried to distant organs, draining lymph nodes and blood, probably via the thoracic duct, with delayed and accumulative translocation to the brain (microglial cells). Brain penetration occurs at extremely low levels in normal conditions, possibly explaining the good tolerance of alum despite its high neurotoxic potential. However, systemic diffusion is considerably enhanced by the potentiating effect of MCP-1, the main monocyte chemoattractant factor, the production of which is subject to marked variations linked to age and to genetic and environmental factors. Selective MCP-1 elevation is the only known circulating biomarker of MMF.

http://www.ncbi.nlm.nih.gov/pubmed/26259285

"Aluminium oxyhydroxide ... has been widely used as a vaccine adjuvant since 1927, but the mechanisms by which it stimulates immune responses remain poorly understood. Although generally well tolerated, alum may occasionally cause chronic health problems in presumably susceptible individuals. Some individuals may rarely develop delayed-onset diffuse myalgia, chronic exhaustion and cognitive dysfunction, associated with long-term persistence (up to 12 years) of alum-loaded macrophages at site of immunization"

From the Journal Clinical Reviews in Allergy Immunology • October 2011

Macrophagic myofaciitis
a vaccine (alum) autoimmune-related disease

Israeli E, Agmon-Levin N, Blank M, Shoenfeld Y.

Center for Autoimmune Diseases, Sheba Medical Center. Tel-Hashomer, Israel

Abstract

Macrophagic myofasciitis (MMF) is an immune-mediated condition first reported in 1998. MMF is characterized by post-vaccination systemic manifestations as well as local-stereotyped and immunologically active lesion in the site of inoculation (deltoid muscle). MMF systemic symptoms included myalgias, arthralgias, marked asthenia, muscle weakness, chronic fatigue, and fever. Recently, studies demonstrated that the local lesion is due to persistence for years at site of injection of an aluminum (Al(OH)3) adjuvant commonly used in human vaccines. Time elapsed from last immunization with an Al(OH)3-containing vaccine to muscle biopsy range from 3 months to 8 years; in rare cases, MMF may be diagnosed even 10 years post-vaccination. The discrepancy between the wide applications of aluminum hydroxide-containing vaccines and the very limited number of MMF cases reported may be resolved by observations suggesting that aluminum-containing vaccinations may trigger MMF in genetically susceptible subjects carrying the HLA-DRB1*01. Thus, MMF may be defined as an emerging novel condition that may be triggered by exposure to alum-containing vaccines, in patients with a specific genetic background, and this temporal association may be exhibited from a few months up to 10 years.

http://www.ncbi.nlm.nih.gov/pubmed/20882368

“Recently, studies demonstrated that the local lesion is due to persistence for years at site of injection of an aluminum (Al(OH)3) adjuvant commonly used in human vaccines”

From the Journal Rheumatology International • January 2015

Macrophagic myofasciitis and vaccination: consequence or coincidence?

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Abstract

Macrophagic myofasciitis (MMF) characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization has been reported with increasing frequency in the past 10 years. We describe clinical and laboratory findings in patients with MMF. We did a retrospective analysis of 16 cases observed in our Neuropathology Laboratory, between January 2000 and July 2013. The mean age of the 16 patients was 48.8 ± 18.0 years; 80.0 % were female. Chronic fatigue syndrome was found in 8 of 16 patients. Half of the patients had elevated creatinine kinase levels, and 25.0 % had a myopathic electromyogram. Thirteen patients received intramuscular administration of aluminum-containing vaccine prior to the onset of symptoms. MMF may mirror a distinctive pattern of an inflammatory myopathy. The vaccines containing this adjuvant may trigger MMF in some patients.

http://www.ncbi.nlm.nih.gov/pubmed/24923906

> “The vaccines containing this adjuvant may trigger MMF in some patients”

From the Journal PLoS One • June 2015

Neuropsychological Correlates of Brain Perfusion SPECT in Patients with Macrophagic Myofasciitis

Van Der Gucht A1, Aoun Sebaiti M2, Itti E1, Aouizerate J3, Evangelista E1, Chalaye J1, Gherardi RK3, Ragunathan-Thangarajah N4, Bachoud-Levi AC5, Authier FJ3.

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Abstract

BACKGROUND:

Patients with aluminum hydroxide adjuvant-induced macrophagic myofasciitis (MMF) complain of arthromyalgias, chronic fatigue and cognitive deficits. This study aimed to characterize brain perfusion in these patients.

METHODS:

Brain perfusion SPECT was performed in 76 consecutive patients (aged 49±10 y) followed in the Garches-Necker-Mondor-Hendaye reference center for rare neuromuscular diseases. Images were acquired 30 min after intravenous injection of 925 MBq 99mTc-ethylcysteinate dimer (ECD) at rest. All patients also underwent a comprehensive battery of neuropsychological tests, within 1.3±5.5 mo from SPECT. Statistical parametric maps (SPM12) were obtained for each test using linear regressions between each performance score and brain perfusion, with adjustment for age, sex, socio-cultural level and time delay between brain SPECT and neuropsychological testing.

RESULTS:

SPM analysis revealed positive correlation between neuropsychological scores (mostly exploring executive functions) and brain perfusion in the posterior associative cortex, including cuneus/precuneus/occipital lingual areas, the periventricular white matter/corpus callosum, and the cerebellum, while negative correlation was found with amygdalo-hippocampal/entorhinal complexes. A positive correlation was also observed between brain perfusion and the posterior associative cortex when the time elapsed since last vaccine injection was investigated.

CONCLUSIONS:

Brain perfusion SPECT showed a pattern of cortical and subcortical changes in accordance with the MMF-associated cognitive disorder previously described. These results provide a neurobiological substrate for brain dysfunction in aluminum hydroxide adjuvant-induced MMF patients.

http://www.ncbi.nlm.nih.gov/pubmed/26030650

> “Patients with aluminum hydroxide adjuvant-induced macrophagic myofasciitis (MMF) complain of arthromyalgias, chronic fatigue and cognitive deficits. This study aimed to characterize brain perfusion in these patients”

From the Journal Frontiers In Neurology • November 2014

Clinical features in patients with long-lasting macrophagic myofasciitis

Rigolet M1, Aouizerate J2, Couette M3,
Ragunathan-Thangarajah N2, Aoun-Sebaiti M3,
Gherardi RK4, Cadusseau J5, Authier FJ4.

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5. Reference Center for Neuromuscular Diseases Garches-Necker-Mondor-Hendaye , Créteil , France ; Paris Est-Créteil University , Créteil , France

Abstract

Macrophagic myofasciitis (MMF) is an emerging condition characterized by specific muscle lesions assessing abnormal long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients usually are middle-aged adults, mainly presenting with diffuse arthromyalgias, chronic fatigue, and marked cognitive deficits, not related to pain, fatigue, or depression. Clinical features usually correspond to that observed in chronic fatigue syndrome/myalgic encephalomyelitis. Representative features of MMF-associated cognitive dysfunction include dysexecutive syndrome, visual memory impairment, and left ear extinction at dichotic listening test. Most patients fulfill criteria for non-amnestic/dysexecutive mild cognitive impairment, even if some cognitive deficits appear unusually severe. Cognitive dysfunction seems stable over time despite marked fluctuations. Evoked potentials may show abnormalities in keeping with central nervous system involvement, with a neurophysiological pattern suggestive of demyelination. Brain perfusion SPECT shows a pattern of diffuse cortical and subcortical abnormalities, with hypoperfusions correlating with cognitive deficiencies. The combination of musculoskeletal pain, chronic fatigue, and cognitive disturbance generates chronic disability with possible social exclusion. Classical therapeutic approaches are usually unsatisfactory making patient care difficult.

http://www.ncbi.nlm.nih.gov/pubmed/25506338

“The combination of musculoskeletal pain, chronic fatigue, and cognitive disturbance generates chronic disability with possible social exclusion. Classical therapeutic approaches are usually unsatisfactory making patient care difficult”

From the Journal Inorganic Biochemistry • November 2011

Long-term follow-up of cognitive dysfunction in patients with aluminum hydroxide-induced macrophagic myofasciitis (MMF)

Passeri E1, Villa C, Couette M, Itti E, Brugieres P,
Cesaro P, Gherardi RK, Bachoud-Levi AC, Authier FJ.

Paris Est-Creteil University & Henri-Mondor University Hospital (APHP):
Reference Center for Neuromuscular Diseases
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Abstract

Macrophagic myofasciitis (MMF) is characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients are middle-aged adults, mainly presenting with diffuse arthromyalgias, chronic fatigue, and cognitive dysfunction. Representative features of MMF-associated cognitive dysfunction (MACD) include (i) dysexecutive syndrome; (i) visual memory; (iii) left ear extinction at dichotic listening test. In present study we retrospectively evaluated the progression of MACD in 30 MMF patients. Most patients fulfilled criteria for non-amnestic/dysexecutive mild cognitive impairment, even if some cognitive deficits seemed unusually severe. MACD remained stable over time, although dysexecutive syndrome tended to worsen. Long-term follow-up of a subset of patients with 3 or 4 consecutive neuropsychological evaluations confirmed the stability of MACD with time, despite marked fluctuations.

http://www.ncbi.nlm.nih.gov/pubmed/22099155

> “Affected patients are middle-aged adults, mainly presenting with diffuse arthromyalgias, chronic fatigue, and cognitive dysfunction”

From the Journal Inorganic Biochemistry • November 2009

Long-term persistence of vaccine-derived aluminum hydroxide is associated with chronic cognitive dysfunction

Couette M1, Boisse MF, Maison P, Brugieres P, Cesaro P, Chevalier X, Gherardi RK, Bachoud-Levi AC, Authier FJ.

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Abstract

Macrophagic myofasciitis (MMF) is an emerging condition, characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients mainly complain of arthromyalgias, chronic fatigue, and cognitive difficulties. We designed a comprehensive battery of neuropsychological tests to prospectively delineate MMF-associated cognitive dysfunction (MACD). Compared to control patients with arthritis and chronic pain, MMF patients had pronounced and specific cognitive impairment. MACD mainly affected (i) both visual and verbal memory; (ii) executive functions, including attention, working memory, and planning; and (iii) left ear extinction at dichotic listening test. Cognitive deficits did not correlate with pain, fatigue, depression, or disease duration. Pathophysiological mechanisms underlying MACD remain to be determined. In conclusion, long-term persistence of vaccine-derived aluminum hydroxide within the body assessed by MMF is associated with cognitive dysfunction, not solely due to chronic pain, fatigue and depression.

http://www.ncbi.nlm.nih.gov/pubmed/19748679

“long-term persistence of vaccine-derived aluminum hydroxide within the body assessed by MMF is associated with cognitive dysfunction”

From the Journal Immunologic Ressearch • December 2014

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA): clues and pitfalls in the pediatric background

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Abstract

The development and increasing diffusion of new vaccinations and global immunization protocols have aroused burning debates about safety of adjuvants and their immunogenicity-enhancing effect in vaccines. Shoenfeld and Agmon-Levin have grouped under the term "autoimmune/inflammatory syndrome induced by adjuvants" (ASIA) a complex of variable signs and symptoms that may occur after a previous exposure to different adjuvants and also external environmental triggers, even eliciting specific overt immune-mediated disorders. This entity subsumes five medical conditions: post-vaccination phenomena, gulf war syndrome, macrophagic myofasciitis syndrome, siliconosis, and sick building syndrome, but the relevance and magnitude of the syndrome in the pediatric age is fundamentally limited to post-vaccination autoimmune or inflammatory disorders. The occurrence of vaccine-triggered phenomena represents a diagnostic challenge for clinicians and a research conundrum for many investigators. In this paper, we will analyze the general features of ASIA and focus on specific post-vaccination events in relation with the pediatric background. In the presence of a favorable genetic background, many autoimmune/inflammatory responses can be triggered by adjuvants and external factors, showing how the man himself might breach immune tolerance and drive many pathogenetic aspects of human diseases. Nonetheless, the elective application of ASIA diagnostic criteria to the pediatric population requires further assessment and evaluations. Additional studies are needed to help clarify connections between innate or adaptive immunity and pathological and/or protective autoantibodies mostly in the pediatric age, as children and adolescents are mainly involved in the immunization agendas related to vaccine-preventable diseases.

http://www.ncbi.nlm.nih.gov/pubmed/25395340

"In the presence of a favorable genetic background, many autoimmune/inflammatory responses can be triggered by adjuvants"

From the Journal Autoimmunity • December 2013

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 2013: Unveiling the pathogenic, clinical and diagnostic aspects

Perricone C, Colafrancesco S, Mazor RD, Soriano A, Agmon-Levin N, Shoenfeld Y.

The Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel; Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Rome, Italy

Abstract

In 2011 a new syndrome termed 'ASIA Autoimmune/Inflammatory Syndrome Induced by Adjuvants' was defined pointing to summarize for the first time the spectrum of immune-mediated diseases triggered by an adjuvant stimulus such as chronic exposure to silicone, tetramethylpentadecane, pristane, aluminum and other adjuvants, as well as infectious components, that also may have an adjuvant effect. All these environmental factors have been found to induce autoimmunity by themselves both in animal models and in humans: for instance, silicone was associated with siliconosis, aluminum hydroxide with post-vaccination phenomena and macrophagic myofasciitis syndrome. Several mechanisms have been hypothesized to be involved in the onset of adjuvant-induced autoimmunity; a genetic favorable background plays a key role in the appearance on such vaccine-related diseases and also justifies the rarity of these phenomena. This paper will focus on protean facets which are part of ASIA, focusing on the roles and mechanisms of action of different adjuvants which lead to the autoimmune/inflammatory response. The data herein illustrate the critical role of environmental factors in the induction of autoimmunity. Indeed, it is the interplay of genetic susceptibility and environment that is the major player for the initiation of breach of tolerance.

http://www.ncbi.nlm.nih.gov/pubmed/24238833

"In 2011 a new syndrome termed 'ASIA' Autoimmune/Inflammatory Syndrome Induced by Adjuvants was defined pointing to summarize for the first time the spectrum of immune-mediated diseases triggered by an adjuvant stimulus such as chronic exposure to ... aluminum and other adjuvants"

From the Journal Autoimmunity • February 2011

'ASIA'
Autoimmune/inflammatory syndrome induced by adjuvants

Shoenfeld Y, Agmon-Levin N.

Abstract

The role of various environmental factors in the pathogenesis of immune mediated diseases is well established. Of which, factors entailing an immune adjuvant activity such as infectious agents, silicone, aluminium salts and others were associated with defined and non-defined immune mediated diseases both in animal models and in humans. In recent years, four conditions: siliconosis, the Gulf war syndrome (GWS), the macrophagic myofasciitis syndrome (MMF) and post-vaccination phenomena were linked with previous exposure to an adjuvant. Furthermore, these four diseases share a similar complex of signs and symptoms which further support a common denominator.Thus, we review herein the current data regarding the role of adjuvants in the pathogenesis of immune mediated diseases as well as the amassed data regarding each of these four conditions. Relating to the current knowledge we would like to suggest to include these comparable conditions under a common syndrome entitled ASIA, "Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants".

http://www.ncbi.nlm.nih.gov/pubmed/20708902

"In recent years, four conditions: siliconosis, the Gulf war syndrome (GWS), the macrophagic myofasciitis syndrome (MMF) and post-vaccination phenomena were linked with previous exposure to an adjuvant"

From the Journal Discovery Medicine • February 2010

Vaccines and autoimmune diseases of the adult

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Abstract

Infectious agents contribute to the environmental factors involved in the development of autoimmune diseases possibly through molecular mimicry mechanisms. Hence, it is feasible that vaccinations may also contribute to the mosaic of autoimmunity. Evidence for the association of vaccinations and the development of these diseases is presented in this review. Infrequently reported post-vaccination autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, inflammatory myopathies, multiple sclerosis, Guillain-Barré syndrome, and vasculitis. In addition, we will discuss macrophagic myofasciitis, aluminum containing vaccines, and the recent evidence for autoimmunity following the use of human papillomavirus vaccine.

http://www.ncbi.nlm.nih.gov/pubmed/20193633

“we will discuss macrophagic myofasciitis, aluminum containing vaccines, and the recent evidence for autoimmunity following the use of human papillomavirus vaccine”

From the Journal Neuropediatrics • August 2009

Macrophagic myofasciitis plus (distinct types of muscular dystrophy)

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Abstract

Macrophagic myofasciitis (MMF) is a well-known lesion following vaccination with aluminium-containing vaccines. It has abundantly been reported in adults and several times in children, often in single patients or in rather small cohorts. Only few of these published reports on children have shown distinct myopathology of another neuromuscular disease except for MMF. Indications for biopsy often were nondescript clinical features in children, such as hypotonia or delay in motor development but, apparently, never that of suspected MMF. Thus, in previous reports as well as in our two patients, encountering MMF in the biopsied tissue specimens was coincidental. Our two unrelated patients with MMF also had two separate types of muscular dystrophy, a merosinopathy and dystrophinopathy, showing a combination of myopathologically well-defined neuromuscular diseases, muscular dystrophies and MMF. Detecting such a combination of two separate conditions may, in the future, be rare when non-invasive techniques, e. g., genetic, will have replaced muscle biopsy in ascertaining hereditary neuromuscular conditions, especially in children.

http://www.ncbi.nlm.nih.gov/pubmed/20135575

“Macrophagic myofasciitis (MMF) is a well-known lesion following vaccination with aluminium-containing vaccines”

From the Journal Lupus • November 2009

Vaccines as a trigger for myopathies

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Abstract

Vaccines are considered to be among the greatest medical discoveries, credited with the virtual eradication of some diseases and the consequent improved survival and quality of life of the at-risk population. With that, vaccines are among the environmental factors implicated as triggers for the development of inflammatory myopathies. The sporadic reports on vaccine-induced inflammatory myopathies include cases of hepatitis B virus, bacillus Calmette-Guérin, tetanus, influenza, smallpox, polio, diphtheria, diphtheria-pertussis-tetanus, combination of diphtheria with scarlet fever and diphtheria-pertussis-tetanus with polio vaccines. However, a significant increase in the incidence of dermatomyositis or polymyositis after any massive vaccination campaign has not been reported in the literature. In study patients with inflammatory myopathies, no recent immunization was recorded in any of the patients. Moreover, after the 1976 mass flu vaccination, no increase in the incidence of inflammatory myopathies was observed. Although rare, macrophagic myofasciitis has been reported following vaccination and is attributed to the aluminium hydroxide used as an adjuvant in some vaccines. Prospective multicenter studies are needed to identify potential environmental factors, including vaccines, as potential triggers for inflammatory myopathies.

http://www.ncbi.nlm.nih.gov/pubmed/19880571

> “vaccines are among the environmental factors implicated as triggers for the development of inflammatory myopathies”

From the Journal Brain • May 2001

Central nervous system disease in patients with macrophagic myofasciitis

Authier FJ, Cherin P, Creange A, Bonnotte B, Ferrer X, Abdelmoumni A, Ranoux D, Pelletier J, Figarella-Branger D, Granel B, Maisonobe T, Coquet M, Degos JD, Gherardi RK.

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Abstract

Macrophagic myofasciitis (MMF), a condition newly recognized in France, is manifested by diffuse myalgias and characterized by highly specific myopathological alterations which have recently been shown to represent an unusually persistent local reaction to intramuscular injections of aluminium-containing vaccines. Among 92 MMF patients recognized so far, eight of them, which included the seven patients reported here, had a symptomatic demyelinating CNS disorder. CNS manifestations included hemisensory or sensorimotor symptoms (four out of seven), bilateral pyramidal signs (six out of seven), cerebellar signs (four out of seven), visual loss (two out of seven), cognitive and behavioural disorders (one out of seven) and bladder dysfunction (one out of seven). Brain T(2)-weighted MRI showed single (two out of seven) or multiple (four out of seven) supratentorial white matter hyperintense signals and corpus callosum atrophy (one out of seven). Evoked potentials were abnormal in four out of six patients and CSF in four out of seven. According to Poser's criteria for multiple sclerosis, the diagnosis was clinically definite (five out of seven) or clinically probable multiple sclerosis (two out of seven). Six out of seven patients had diffuse myalgias. Deltoid muscle biopsy showed stereotypical accumulations of PAS (periodic acid-Schiff)-positive macrophages, sparse CD8+ T cells and minimal myofibre damage. Aluminium-containing vaccines had been administered 3-78 months (median = 33 months) before muscle biopsy (hepatitis B virus: four out of seven, tetanus toxoid: one out of seven, both hepatitis B virus and tetanus toxoid: two out of seven). The association between MMF and multiple sclerosis-like disorders may give new insights into the controversial issues surrounding vaccinations and demyelinating CNS disorders. Deltoid muscle biopsy searching for myopathological alterations of MMF should be performed in multiple sclerosis patients with diffuse myalgias.

http://www.ncbi.nlm.nih.gov/pubmed/11335699

"The association between MMF and multiple sclerosis-like disorders may give new insights into the controversial issues surrounding vaccinations and demyelinating CNS disorders"

From the Journal of Autoimmunity • November 2014

Immunization with hepatitis B vaccine accelerates SLE-like disease in a murine [mouse] model

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Abstract

Hepatitis-B vaccine (HBVv) can prevent HBV-infection and associated liver diseases. However, concerns regarding its safety, particularly among patients with autoimmune diseases (i.e. SLE) were raised. Moreover, the aluminum adjuvant in HBVv was related to immune mediated adverse events. Therefore, we examined the effects of immunization with HBVv or alum on SLE-like disease in a murine model. NZBWF1 mice were immunized with HBVv (Engerix), or aluminum hydroxide (alum) or phosphate buffered saline (PBS) at 8 and 12 weeks of age. Mice were followed for weight, autoantibodies titers, blood counts, proteinuria, kidney histology, neurocognitive functions (novel object recognition, staircase, Y-maze and the forced swimming tests) and brain histology. Immunization with HBVv induced acceleration of kidney disease manifested by high anti-dsDNA antibodies ($p < 0.01$), early onset of proteinuria ($p < 0.05$), histological damage and deposition of HBs antigen in the kidney. Mice immunized with HBVv and/or alum had decreased cells counts mainly of the red cell lineage ($p < 0.001$), memory deficits ($p < 0.01$), and increased activated microglia in different areas of the brain compare with mice immunized with PBS. Anxiety-like behavior was more pronounced among mice immunized with alum. In conclusion, herein we report that immunization with the HBVv aggravated kidney disease in an animal model of SLE. Immunization with either HBVv or alum affected blood counts, neurocognitive functions and brain gliosis. Our data support the concept that different component of vaccines may be linked with immune and autoimmune mediated adverse events.

http://www.ncbi.nlm.nih.gov/pubmed/25042822

“Our data support the concept that different component of vaccines may be linked with immune and autoimmune mediated adverse events”

From the Journal Autoimmunity Reviews • October 2015

On vaccine's adjuvants and autoimmunity: Current evidence and future perspectives

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Abstract

Adjuvants are compounds incorporated into vaccines to enhance immunogenicity and the development of these molecules has become an expanding field of research in the last decades. Adding an adjuvant to a vaccine antigen leads to several advantages, including dose sparing and the induction of a more rapid, broader and strong immune response. Several of these molecules have been approved, including aluminium salts, oil-in-water emulsions (MF59, AS03 and AF03), virosomes and AS04. Adjuvants have recently been implicated in the new syndrome named "ASIA-Autoimmune/inflammatory Syndrome Induced by Adjuvants", which describes an umbrella of clinical conditions including post-vaccination adverse reactions. Recent studies implicate a web of mechanisms in the development of vaccine adjuvant-induced autoimmune diseases, in particular, in those associated with aluminium-based compounds. Fewer and unsystematised data are instead available about other adjuvants, despite recent evidence indicating that vaccines with different adjuvants may also cause specific autoimmune adverse reactions possible towards different pathogenic mechanisms. This topic is of importance as the specific mechanism of action of each single adjuvant may have different effects on the course of different diseases. Herein, we review the current evidence about the mechanism of action of currently employed adjuvants and discuss the mechanisms by which such components may trigger autoimmunity.

http://www.ncbi.nlm.nih.gov/pubmed/26031899

"we ... discuss the mechanisms by which such components may trigger autoimmunity"

From the Journal Clinical and Experimental Rheumatology • July 2015

Autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA) after quadrivalent human papillomavirus vaccination in Colombians: a call for personalised medicine

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Abstract

This was a case study in which 3 patients with autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA) after quadrivalent human papillomavirus vaccination (HPV) were evaluated and described. All the patients were women. Diagnosis consisted of HLA-B27 enthesitis related arthritis, rheumatoid arthritis and systemic lupus erythematous, respectively. Our results highlight the risk of developing ASIA after HPV vaccination and may serve to increase the awareness of such a complication. Factors that are predictive of developing autoimmune diseases should be examined at the population level in order to establish preventive measures in at-risk individuals for whom healthcare should be personalized and participatory.

http://www.ncbi.nlm.nih.gov/pubmed/25962455

> “Our results highlight the risk of developing ASIA after HPV vaccination”

From the Journal Immunologic Research • December 2014

Chronic fatigue syndrome and fibromyalgia following immunization with the hepatitis B vaccine: another angle of the 'autoimmune (auto-inflammatory) syndrome induced by adjuvants' (ASIA)

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Abstract

The objectives of this study were to gather information regarding demographic and clinical characteristics of patients diagnosed with either fibromyalgia (FM) or chronic fatigue (CFS) following hepatitis B vaccination (HBVv) and furthermore to apply the recently suggested criteria of autoimmune (auto-inflammatory) syndromes induced by adjuvants (ASIA), in the aim of identifying common characteristics that may suggest an association between fibromyalgia, chronic fatigue and HBV vaccination. Medical records of 19 patients with CFS and/or fibromyalgia following HBVv immunization were analyzed. All of which were immunized during 1990-2008 in different centers in the USA. All medical records were evaluated for demographics, medical history, the number of vaccine doses, as well as immediate and long term post-immunization adverse events and clinical manifestations. In addition, available blood tests, imaging results, treatments and outcomes were analyzed. ASIA criteria were applied to all patients. The mean age of patients was 28.6 ± 11 years, of which 68.4 % were females. 21.05 % had either personal or familial background of autoimmune disease. The mean latency period from the last dose of HBVv to onset of symptoms was 38.6 ± 79.4 days, ranging from days to a year. Eight (42.1 %) patients continued with the immunization program despite experiencing adverse events. Manifestations that were commonly reported included neurological manifestations (84.2 %), musculoskeletal (78.9 %), psychiatric (63.1 %), fatigue (63.1 %), gastrointestinal complains (58 %) and mucocutaneous manifestations (36.8 %). Autoantibodies were detected in 71 % of patients tested. All patients fulfilled the ASIA criteria. This study suggests that in some cases CFS and FM can be temporally related to immunization, as part of ASIA syndrome. The appearance of adverse event during immunization, the presence of autoimmune susceptibility and higher titers of autoantibodies all can be suggested as risk factors. ASIA criteria were fulfilled in all patients eluding the plausible link between ASIA and CFS/FM.

http://www.ncbi.nlm.nih.gov/pubmed/25427994

"The objectives of this study were to gather information regarding demographic and clinical characteristics of patients diagnosed with either fibromyalgia (FM) or chronic fatigue (CFS) following hepatitis B vaccination"

From the Journal Immunologic Research • December 2014

A sudden onset of a pseudo-neurological syndrome after HPV-16/18 AS04-adjuvated vaccine: might it be an autoimmune/inflammatory syndrome induced by adjuvants (ASIA) presenting as a somatoform disorder?

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Abstract

In last centuries, vaccines reduced the incidence of several infectious diseases. In last decades, some vaccines aimed at preventing also some cancers, where viruses play a causative role. However, several adverse events have been described after vaccines, but a causal relationship has been established only in a minority of cases. Here, we describe a pseudo-neurological syndrome occurred shortly after the administration of the bivalent HPV vaccine. Some autoimmune disorders, including neurological demyelinating diseases, have been reported after HPV vaccines, but the patient showed no organic lesions. The patient was diagnosed as having a functional somatoform syndrome, which was supposed to be autoimmune/inflammatory syndrome induced by adjuvants (ASIA), seen the temporal link with vaccination and the presence of anti-phospholipid autoantibodies. Immunological mechanisms of vaccines-and of adjuvants-have not been completely elucidated yet, and although there is no evidence of statistical association with many post-vaccination events, a causal link with vaccine cannot be excluded in some individuals.

http://www.ncbi.nlm.nih.gov/pubmed/25388965

> “Here, we describe a pseudo-neurological syndrome occurred shortly after the administration of the bivalent HPV vaccine”

From the Journal Immunologic Research • February 2015

The epidemiological profile of ASIA syndrome after HPV vaccination: an evaluation based on the Vaccine Adverse Event Reporting Systems

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Abstract

The term "ASIA-Autoimmune/inflammatory Syndrome Induced by Adjuvants" describes an umbrella of clinical conditions sharing similar signs or symptoms, including post-vaccination phenomena. No information is available on the epidemiology of the ASIA syndrome, especially following HPV vaccination. We carried out an analysis of the VAERS database to retrieve all cases of suspected ASIA syndrome according to the Shoenfeld and Agmon-Levin's guideline for the diagnosis. After causality assessment and case validation, 2,207 cases were considered probably or possibly related to vaccination. These represent the largest ASIA cohort ever reported and allowed us to estimate epidemiological and clinical characteristic of this syndrome. The commonest clinical manifestation observed were pyrexia (58%), myalgia (27%) and arthralgia or arthritis (19%), and the estimated reporting rate was of 3.6 cases per 100,000 doses of HPV vaccine distributed (95% CI 3.4-3.7). This study presents the first systematic estimation of ASIA incidence and expands the knowledge on this pathology. Further analyses are needed to identify genetic and non-genetic risk factors for ASIA syndrome.

http://www.ncbi.nlm.nih.gov/pubmed/25381482

"After causality assessment and case validation, **2207** cases were considered probably or possibly related to vaccination"

Ways Sjögren's syndrome may affect the body

From the Journal of Autoimmunity • June 2014

Sjögren's syndrome: another facet of the autoimmune/inflammatory syndrome induced by adjuvants (ASIA)

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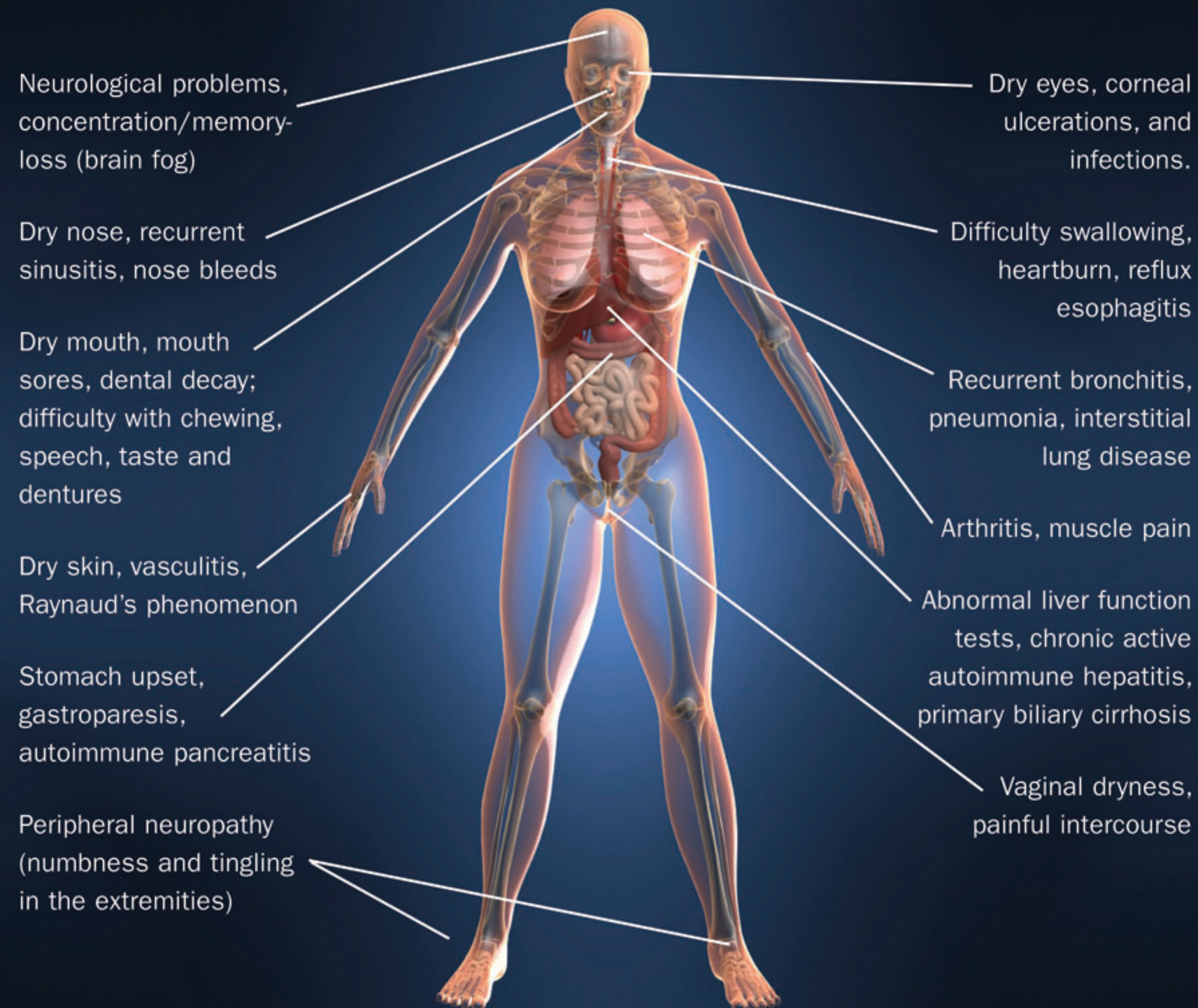
Abstract

Recently, a new syndrome, namely the "Autoimmune/inflammatory syndrome induced by adjuvants" (ASIA) has been defined. In this syndrome different conditions characterized by common signs and symptoms and induced by the presence of an adjuvant are included. The adjuvant is a substance capable of boosting the immune response and of acting as a trigger in the development of autoimmune diseases. Post-vaccination autoimmune phenomena represent a major issue of ASIA. Indeed, despite vaccines represent a mainstay in the improvement of human health, several of these have been implicated as a potential trigger for autoimmune diseases. Sjogren's Syndrome (SjS) is a systemic chronic autoimmune inflammatory disease characterized by the presence of an inflammatory involvement of exocrine glands accompanied by systemic manifestations. Own to the straight association between infectious agents exposure (mainly viruses) and sicca syndrome development, the possible link between vaccine and SjS is not surprising. Indeed, a few cases of SjS following vaccine delivery have been reported. At the same extent, the induction of SjS following silicone exposure has been described too. Thus, the aim of this review was to focus on SjS and its possible development following vaccine or silicone exposure in order to define another possible facet of the ASIA syndrome.

http://www.ncbi.nlm.nih.gov/pubmed/24774584



From the Journal Clinical And Experimental Rheumatology • March 2014

Alum, an aluminum-based adjuvant, induces Sjögren's syndrome-like disorder in mice

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Abstract

OBJECTIVES:
Adjuvant-induced innate immune responses have been suspected to play a role in the initiation of certain autoimmune disorders. This study investigates the role of alum, an aluminum-based adjuvant in the induction of Sjögren's syndrome-like disorder in mice.

METHODS:
Inbred, female New Zealand Mixed (NZM) 2758 strain of mice were injected with alum. Control mice were treated similarly with PBS. The mice were monitored for salivary gland dysfunction by measuring pilocarpine-induced salivation. Presence of lymphocytic infiltrates within the submandibular glands was studied by histopathology. Autoantibodies to Ro and La proteins were analysed by ELISA and the presence of anti-nuclear antibodies (ANA) was analysed by indirect immunofluorescence.

RESULTS:
By eight weeks after treatment, the saliva production in the alum-treated mice was significantly decreased in comparison to the PBS-treated mice. This functional loss persisted till the termination of experiments at 20 wks. The incidence and severity of sialoadenitis was significantly higher in the alum-treated mice. Although there were no differences in the levels of anti-Ro/La autoantibodies in sera of alum and PBS-treated groups, the alum group showed higher ANA reactivity.

CONCLUSIONS:
In the NZM2758 mice, alum induces a Sjögren's syndrome-like disorder that is characterised by chronic salivary gland dysfunction and the presence of lymphocytic infiltrates within the salivary glands. Thus, the potential of aluminum-based adjuvants for induction of autoimmunity should be closely monitored in individuals genetically susceptible to developing autoimmune disorders.

http://www.ncbi.nlm.nih.gov/pubmed/24739520

"the potential of aluminum-based adjuvants for induction of autoimmunity should be closely monitored in individuals genetically susceptible to developing autoimmune disorders"

From the Journal Of Investigative Medicine High Impact Case Reports • March 2014

Postural Orthostatic Tachycardia With Chronic Fatigue After HPV Vaccination as Part of the Autoimmune/Auto-inflammatory Syndrome Induced by Adjuvants: Case Report and Literature Review

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Abstract

We report the case of a 14-year-old girl who developed postural orthostatic tachycardia syndrome (POTS) with chronic fatigue 2 months following Gardasil vaccination. The patient suffered from persistent headaches, dizziness, recurrent syncope, poor motor coordination, weakness, fatigue, myalgias, numbness, tachycardia, dyspnea, visual disturbances, phonophobia, cognitive impairment, insomnia, gastrointestinal disturbances, and a weight loss of 20 pounds. The psychiatric evaluation ruled out the possibility that her symptoms were psychogenic or related to anxiety disorders. Furthermore, the patient tested positive for ANA (1:1280), lupus anticoagulant, and antiphospholipid. On clinical examination she presented livedo reticularis and was diagnosed with Raynaud's syndrome. This case fulfills the criteria for the autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA). Because human papillomavirus vaccination is universally recommended to teenagers and because POTS frequently results in long-term disabilities (as was the case in our patient), a thorough follow-up of patients who present with relevant complaints after vaccination is strongly recommended.

http://www.ncbi.nlm.nih.gov/pubmed/26425598

> "This case fulfills the criteria for ... Postural Orthostatic Tachycardia with Chronic Fatigue after HPV Vaccination ... induced by adjuvants"

From the Journal Current Medicinal Chemistry • 2013

Autoimmune (auto-inflammatory) syndrome induced by adjuvants (ASIA) animal models as a proof of concept

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Abstract

ASIA syndrome, "Autoimmune (Auto-inflammatory) Syndromes Induced by Adjuvants" includes at least four conditions which share a similar complex of signs and symptoms and have been defined by hyperactive immune responses: siliconosis, macrophagic myofasciitis syndrome, Gulf war syndrome and post-vaccination phenomena. Exposure to adjuvants has been documented in these four medical conditions, suggesting that the common denominator to these syndromes is a trigger entailing adjuvant activity. An important role of animal models in proving the ASIA concept has been established. Experimentally animal models of autoimmune diseases induced by adjuvants are currently widely used to understand the mechanisms and etiology and pathogenesis of these diseases and might thus promote the development of new diagnostic, predictive and therapeutic methods. In the current review we wish to unveil the variety of ASIA animal models associated with systemic and organ specific autoimmune diseases induced by adjuvants. We included in this review animal models for rheumatoid arthritis-like disease, for systemic lupus erythematosus-like disease, autoimmune thyroid disease-like disease, antiphospholipid syndrome, myocarditis and others. All these models support the concept of ASIA, as the Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants.

http://www.ncbi.nlm.nih.gov/pubmed/23992328

"We included in this review ... rheumatoid arthritis-like disease ... systemic lupus erythematosus-like disease, autoimmune thyroid disease-like disease, antiphospholipid syndrome, myocarditis and others ... All these models support the concept of ASIA, as the Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants"

From the American Journal Of Reproductive Immunology • October 2013

Human papilloma virus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants

Colafrancesco S, Perricone C, Tomljenovic L, Shoenfeld Y.

Abstract

PROBLEM:

Post-vaccination autoimmune phenomena are a major facet of the autoimmune/inflammatory syndrome induced by adjuvants (ASIA) and different vaccines, including HPV, have been identified as possible causes.

METHOD OF STUDY:

The medical history of three young women who presented with secondary amenorrhea following HPV vaccination was collected. Data regarding type of vaccine, number of vaccination, personal, clinical and serological features, as well as response to treatments were analyzed.

RESULTS:

All three patients developed secondary amenorrhea following HPV vaccinations, which did not resolve upon treatment with hormone replacement therapies. In all three cases sexual development was normal and genetic screen revealed no pertinent abnormalities (i.e., Turner's syndrome, Fragile X test were all negative). Serological evaluations showed low levels of estradiol and increased FSH and LH and in two cases, specific auto-antibodies were detected (antiovarian and anti thyroid), suggesting that the HPV vaccine triggered an autoimmune response. Pelvic ultrasound did not reveal any abnormalities in any of the three cases. All three patients experienced a range of common non-specific post-vaccine symptoms including nausea, headache, sleep disturbances, arthralgia and a range of cognitive and psychiatric disturbances. According to these clinical features, a diagnosis of primary ovarian failure (POF) was determined which also fulfilled the required criteria for the ASIA syndrome.

CONCLUSION:

We documented here the evidence of the potential of the HPV vaccine to trigger a life-disabling autoimmune condition. The increasing number of similar reports of post HPV vaccine-linked autoimmunity and the uncertainty of long-term clinical benefits of HPV vaccination are a matter of public health that warrants further rigorous inquiry.

http://www.ncbi.nlm.nih.gov/pubmed/23902317

"We documented here the evidence of the potential of the HPV vaccine to trigger a life-disabling autoimmune condition. The increasing number of similar reports of post HPV vaccine-linked autoimmunity and the uncertainty of long-term clinical benefits of HPV vaccination are a matter of public health that warrants further rigorous inquiry"

From the Journal Immunologic Research • July 2013

Adverse events following immunization with vaccines containing adjuvants

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Abstract

A traditional infectious disease vaccine is a preparation of live attenuated, inactivated or killed pathogen that stimulates immunity. Vaccine immunologic adjuvants are compounds incorporated into vaccines to enhance immunogenicity. Adjuvants have recently been implicated in the new syndrome named ASIA autoimmune/inflammatory syndrome induced by adjuvants. The objective describes the frequencies of post-vaccination clinical syndrome induced by adjuvants. We performed a cross-sectional study; adverse event following immunization was defined as any untoward medical occurrence that follows immunization 54 days prior to the event. Data on vaccinations and other risk factors were obtained from daily epidemiologic surveillance. Descriptive statistics were done using means and standard deviation, and odds ratio adjusted for potential confounding variables was calculated with SPSS 17 software. Forty-three out of 120 patients with moderate or severe manifestations following immunization were hospitalized from 2008 to 2011. All patients fulfilled at least 2 major and 1 minor criteria suggested by Shoenfeld and Agmon-Levin for ASIA diagnosis. The most frequent clinical findings were pyrexia 68%, arthralgias 47%, cutaneous disorders 33%, muscle weakness 16% and myalgias 14%. Three patients had diagnosis of Guillain-Barre syndrome, one patient had Adult-Still's disease 3 days after vaccination. A total of 76% of the events occurred in the first 3 days post-vaccination. Two patients with previous autoimmune disease showed severe adverse reactions with the reactivation of their illness. Minor local reactions were present in 49% of patients. Vaccines containing adjuvants may be associated with an increased risk of autoimmune/inflammatory adverse events following immunization.

http://www.ncbi.nlm.nih.gov/pubmed/23576057

"Forty-three out of 120 patients with moderate or severe manifestations following immunization were hospitalized from 2008 to 2011. All patients fulfilled at least 2 major and 1 minor criteria suggested by Shoenfeld and Agmon-Levin for ASIA diagnosis"

From BMC Medicine • April 2013

Novel pebbles in the mosaic of autoimmunity

Perricone C, Agmon-Levin N, Shoenfeld Y.

Abstract

Almost 25 years ago, the concept of the 'mosaic of autoimmunity' was introduced to the scientific community, and since then this concept has continuously evolved, with new pebbles being added regularly. We are now looking at an era in which the players of autoimmunity have changed names and roles. In this issue of BMC Medicine, several aspects of autoimmunity have been addressed, suggesting that we are now at the forefront of autoimmunity science. Within the environmental factors generating autoimmunity are now included unsuspected molecules such as vitamin D and aluminum. Some adjuvants such as aluminum are recognized as causal factors in the development of the autoimmune response. An entirely new syndrome, the autoimmune/inflammatory syndrome induced by adjuvants (ASIA), has been recently described. This is the new wind blowing within the branches of autoimmunity, adding knowledge to physicians for helping patients with autoimmune disease.

http://www.ncbi.nlm.nih.gov/pubmed/23557479

"Some adjuvants such as aluminum are recognized as causal factors in the development of the autoimmune response"

From Expert Review Of Clinical Immunology • April 2013

Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome): clinical and immunological spectrum

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Abstract

An adjuvant is a substance that enhances the antigen-specific immune response, induces the release of inflammatory cytokines, and interacts with Toll-like receptors and the NALP3 inflammasome. The immunological consequence of these actions is to stimulate the innate and adaptive immune response. The activation of the immune system by adjuvants, a desirable effect, could trigger manifestations of autoimmunity or autoimmune disease. Recently, a new syndrome was introduced, autoimmune/inflammatory syndrome induced by adjuvants (ASIA), that includes postvaccination phenomena, macrophagic myofasciitis, Gulf War syndrome and siliconosis. This syndrome is characterized by nonspecific and specific manifestations of autoimmune disease. The main substances associated with ASIA are squalene (Gulf War syndrome), aluminum hydroxide (postvaccination phenomena, macrophagic myofasciitis) and silicone with siliconosis. Mineral oil, guaiacol and iodine gadital are also associated with ASIA. The following review describes the wide clinical spectrum and pathogenesis of ASIA including defined autoimmune diseases and nonspecific autoimmune manifestations, as well as the outlook of future research in this field.

http://www.ncbi.nlm.nih.gov/pubmed/23557271

> "The activation of the immune system by adjuvants, a desirable effect, could trigger manifestations of autoimmunity or autoimmune disease"

From the BMC Medical Journal • April 2013

Slow CCL2-dependent translocation of biopersistent particles from muscle to brain

Khan Z, Combadière C, Authier FJ, Itier V, Lux F, Exley C, Mahrouf-Yorgov M, Decrouy X, Moretto P, Tillement O, Gherardi RK, Cadusseau J.

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> “continuously escalating doses of this poorly biodegradable adjuvant in the population may become insidiously unsafe”

Abstract

BACKGROUND:
Long-term biodistribution of nanomaterials used in medicine is largely unknown. This is the case for alum, the most widely used vaccine adjuvant, which is a nanocrystalline compound spontaneously forming micron/submicron-sized agglomerates. Although generally well tolerated, alum is occasionally detected within monocyte-lineage cells long after immunization in presumably susceptible individuals with systemic/neurologic manifestations or autoimmune (inflammatory) syndrome induced by adjuvants (ASIA).

METHODS:
On the grounds of preliminary investigations in 252 patients with alum-associated ASIA showing both a selective increase of circulating CCL2, the major monocyte chemoattractant, and a variation in the CCL2 gene, we designed mouse experiments to assess biodistribution of vaccine-derived aluminum and of alum-particle fluorescent surrogates injected in muscle. Aluminum was detected in tissues by Morin stain and particle induced X-ray emission) (PIXE) Both 500 nm fluorescent latex beads and vaccine alum agglomerates-sized nanohybrids (Al-Rho) were used.

RESULTS:
Intramuscular injection of alum-containing vaccine was associated with the appearance of aluminum deposits in distant organs, such as spleen and brain where they were still detected one year after injection. Both fluorescent materials injected into muscle translocated to draining lymph nodes (DLNs) and thereafter were detected associated with phagocytes in blood and spleen. Particles linearly accumulated in the brain up to the six-month endpoint; they were first found in perivascular CD11b+ cells and then in microglia and other neural cells. DLN ablation dramatically reduced the biodistribution. Cerebral translocation was not observed after direct intravenous injection, but significantly increased in mice with chronically altered blood-brain-barrier. Loss/gain-of-function experiments consistently implicated CCL2 in systemic diffusion of Al-Rho particles captured by monocyte-lineage cells and in their subsequent neurodelivery. Stereotactic particle injection pointed out brain retention as a factor of progressive particle accumulation.

CONCLUSION:
Nanomaterials can be transported by monocyte-lineage cells to DLNs, blood and spleen, and, similarly to HIV, may use CCL2-dependent mechanisms to penetrate the brain. This occurs at a very low rate in normal conditions explaining good overall tolerance of alum despite its strong neurotoxic potential. However, continuously escalating doses of this poorly biodegradable adjuvant in the population may become insidiously unsafe, especially in the case of overimmunization or immature/altered blood brain barrier or high constitutive CCL-2 production.

http://www.ncbi.nlm.nih.gov/pubmed/23557144

“Al is a potential factor for the induction of inflammation in CD [Crohn’s Disease]”

From the Journal Lupus • February 2012

Aluminum as an adjuvant in Crohn’s disease induction

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Abstract

Alum (AlK(SO(4))(2)) is an adjuvant commonly utilized in vaccines, and is a ubiquitous element used extensively in contemporary life. Food, air, water, waste, the earth’s surface, and pharmaceuticals all represent pathways of aluminum (Al) exposure. Crohn’s disease (CD) is a chronic relapsing intestinal inflammation in genetically susceptible individuals and is caused by yet unidentified environmental factors. Al is a potential factor for the induction of inflammation in CD, and its immune activities share many characteristics with the immune pathology of CD: many luminal bacterial or dietary compounds can be adsorbed to the metal surface and induce Th1 profile cytokines, shared cytokines/chemokines, co-stimulatory molecules, and intracellular pathways and stress-related molecular expression enhancement, affecting intestinal macrobiota, trans-mural granuloma formation, and colitis induction in an animal CD model. The inflammasome plays a central role in Al mode of action and in CD pathophysiology. It is suggested that Al adjuvant activity can fit between the aberrations of innate and adaptive immune responses occurring in CD. The CD mucosa is confronted with numerous inappropriate bacterial components adsorbed on the Al compound surface, constituting a pro-inflammatory supra-adjuvant. Al fits the diagnostic criteria of the newly described autoimmune/inflammatory syndrome induced by adjuvants. If a cause and effect relationship can be established, the consequences will greatly impact public health and CD prevention and management.

http://www.ncbi.nlm.nih.gov/pubmed/22235058

Adjuvant immunization induces high levels of pathogenic antiphospholipid antibodies in genetically prone mice: another facet of the ASIA syndrome

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Abstract

Adjuvants may induce autoimmune diseases in susceptible individuals, a phenomenon recently defined as autoimmune/inflammatory syndrome induced by adjuvants (ASIA). Patients with both antiphospholipid antibodies (aPL) and the genetic coagulopathy factor V Leiden (FVL) are frequently found. We therefore evaluated whether adjuvant can induce aPL in heterozygous FVL mice. aPL were measured in naïve mice and at 1 and 5 months after immunization with either complete or incomplete Freund's adjuvant (CFA, IFA) in FVL and control C57/B6 background mice. We defined antibody levels 3 SD above the mean of C57/B6 mice immunized with adjuvant as positive (specificity of 99%). For □(2)GPI-dependent aPL, 28.6% (6/21) of FVL mice 5 months after immunization with adjuvant (both IFA and CFA) were positive compared with 4.8% (1/22) of FVL mice 1 month after adjuvant and 0% of naïve FVL and C57/B6 mice (0/16, $p < 0.001$). aPL levels correlated with behavioral hyperactivity in the staircase test. FVL mice immunized with adjuvant did not develop □(2)GPI-independent aPL. We hypothesize that the FVL aPL association is not a coincidence, but that chronic coagulation defects combined with external inflammatory stimuli analogous to adjuvant may induce aPL and also antiphospholipid syndrome, thus supporting the notion of ASIA.

http://www.ncbi.nlm.nih.gov/pubmed/22235055

> “Adjuvants may induce autoimmune diseases in susceptible individuals”

Induction of the ‘ASIA’ syndrome in NZB/NZWF1 mice after injection of complete Freund’s adjuvant (CFA)

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Abstract

Adjuvants, commonly used in vaccines, may be responsible for inducing autoimmunity and autoimmune diseases, both in humans and mice. The so-called ‘ASIA’ (Autoimmune/inflammatory Syndrome Induced by Adjuvants) syndrome has been recently described, which is caused by the exposure to a component reproducing the effect of adjuvants. The aim of our study was to evaluate the effect of injection of complete Freund’s adjuvant (CFA) in NZB/NZWF1 mice, a lupus-prone murine model. We injected 10 NZB/NZWF1 mice with CFA/PBS and 10 with PBS, three times, 3 weeks apart, and followed-up until natural death. CFA-injected mice developed both anti-double-stranded DNA and proteinuria earlier and at higher levels than the control group. Proteinuria-free survival rate and survival rate were significantly lower in CFA-treated mice than in the control mice ($p = 0.002$ and $p = 0.001$, respectively). Histological analyses showed a more severe glomerulonephritis in CFA-injected mice compared with the control mice. In addition, lymphoid hyperplasia in spleen and lungs, myocarditis, and vasculitis were observed in the former, but not in the latter group. In conclusion, the injection of CFA in NZB/NZWF1 mice accelerated autoimmune manifestations resembling ‘ASIA’ syndrome in humans.

http://www.ncbi.nlm.nih.gov/pubmed/22235054

> “Adjuvants, commonly used in vaccines, may be responsible for inducing autoimmunity and autoimmune diseases, both in humans and mice”

From the Journal Lupus • February 2012

Gulf War syndrome as a part of the autoimmune (autoinflammatory) syndrome induced by adjuvant (ASIA)

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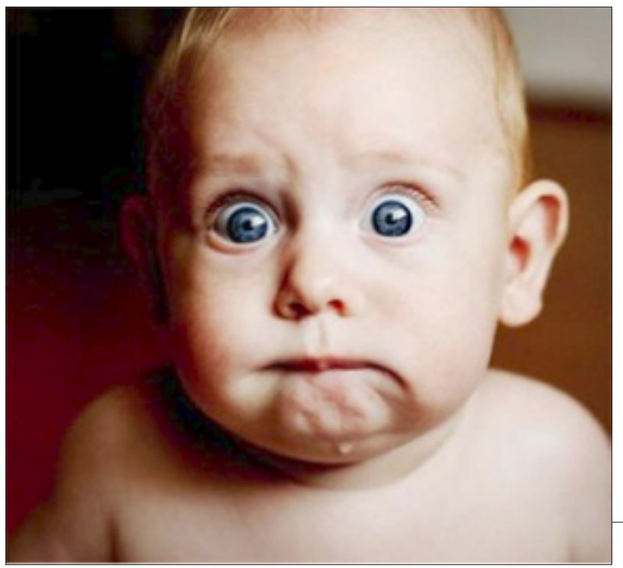
Abstract

Gulf War syndrome (GWS) is a multi-symptom condition comprising a variety of signs and symptoms described in the literature, which not been fully resolved. The various symptoms of the condition include muscle fatigue and tiredness, malaise, myalgia, impaired cognition, ataxia, diarrhoea, bladder dysfunction, sweating disturbances, headaches, fever, arthralgia, skin rashes, and gastrointestinal and sleep disturbances. In addition, excessive chemical sensitivity and odour intolerance is reported. The aetiology of the condition is unclear, but many reviews and epidemiological analyses suggest association with pyridostigmine bromide (PB), certain vaccination regimes, a variety of possible chemical exposures, including smoke from oil-well fires or depleted uranium from shells, as well as physical and psychological stress. Recently, Shoenfeld et al. suggested that four conditions--siliconosis, macrophagic myofaciitis (MMF), GWS and post-vaccination phenomena--that share clinical and pathogenic resemblances, may be incorporated into common syndrome called 'Autoimmune (Autoinflammatory) Syndrome induced by Adjuvants' (ASIA). Symptoms and signs of the four conditions described by Shoenfeld et al. show that at least eight out of ten main symptoms are in correlation in all four conditions. Namely, myalgia, arthralgias, chronic fatigue, neurological cognitive impairment, gastrointestinal symptoms, respiratory symptoms, skin manifestations and appearance of autoantibodies. Regardless of the aetiology of GWS, be it exposure to environmental factors or chemical drugs, vaccinations or the adjuvants in them, GWS fits well with the definition of ASIA and is included as part of 'Shoenfeld's syndrome'.

http://www.ncbi.nlm.nih.gov/pubmed/22235052

"Regardless of the aetiology of GWS, be it exposure to environmental factors or chemical drugs, vaccinations or the adjuvants in them, GWS fits well with the definition of ASIA and is included as part of 'Shoenfeld's syndrome'"



From the Journal Lupus • February 2012

Giant cell arteritis and polymyalgia rheumatica after influenza vaccination: report of 10 cases and review of the literature

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Abstract

Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are inflammatory rheumatic diseases common in people over the age of 50 years. Herein, we report 10 cases of previously healthy subjects who developed GCA/PMR within 3 months of influenza vaccination (Inf-V). A Medline search uncovered additional 11 isolated cases of GCA/PMR occurring after Inf-V. We discuss the role of individual susceptibility, the potential function of immune adjuvants as triggers of autoimmunity post-vaccination, and the correlation of our observation with the 'ASIA' syndrome, i.e. autoimmune/inflammatory syndrome induced by adjuvants and including post-vaccination phenomena.

http://www.ncbi.nlm.nih.gov/pubmed/22235046

"Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are inflammatory rheumatic diseases common in people over the age of 50 years. Herein, we report 10 cases of previously healthy subjects who developed GCA/PMR within 3 months of influenza vaccination"

From the Journal Lupus • February 2012

Autoimmunity following hepatitis B vaccine as part of the spectrum of 'Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants' (ASIA): analysis of 93 cases

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Abstract

OBJECTIVES:

In this study we analyzed the clinical and demographic manifestations among patients diagnosed with immune/autoimmune-mediated diseases post-hepatitis B vaccination. We aimed to find common denominators for all patients, regardless of different diagnosed diseases, as well as the correlation to the criteria of Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants (ASIA).

PATIENTS AND METHODS:

We have retrospectively analyzed the medical records of 114 patients, from different centers in the USA, diagnosed with immune-mediated diseases following immunization with hepatitis-B vaccine (HBVv). All patients in this cohort sought legal consultation. Of these, 93/114 patients diagnosed with disease before applying for legal consultation were included in the study. All medical records were evaluated for demographics, medical history, number of vaccine doses, peri-immunization adverse events and clinical manifestations of diseases. In addition, available blood tests, imaging results, treatments and outcomes were recorded. Signs and symptoms of the different immune-mediated diseases were grouped according to the organ or system involved. ASIA criteria were applied to all patients.

RESULTS:

The mean age of 93 patients was 26.5 ± 15 years; 69.2% were female and 21% were considered autoimmune susceptible. The mean latency period from the last dose of HBVv and onset of symptoms was 43.2 days. Of note, 47% of patients continued with the immunization program despite experiencing adverse events. Manifestations that were commonly reported included neuro-psychiatric (70%), fatigue (42%) mucocutaneous (30%), musculoskeletal (59%) and gastrointestinal (50%) complaints. Elevated titers of autoantibodies were documented in 80% of sera tested. In this cohort 80/93 patients (86%), comprising 57/59 (96%) adults and 23/34 (68%) children, fulfilled the required criteria for ASIA.

CONCLUSIONS:

Common clinical characteristics were observed among 93 patients diagnosed with immune-mediated conditions post-HBVv, suggesting a common denominator in these diseases. In addition, risk factors such as history of autoimmune diseases and the appearance of adverse event(s) during immunization may serve to predict the risk of post-immunization diseases. The ASIA criteria were found to be very useful among adults with post-vaccination events. The application of the ASIA criteria to pediatric populations requires further study.

http://www.ncbi.nlm.nih.gov/pubmed/22235045

"Common clinical characteristics were observed among 93 patients diagnosed with immune-mediated conditions post-HBVv [vaccine], suggesting a common denominator in these diseases"

“Some adjuvants may exert adverse effects upon injection or, on the other hand, may not trigger a full immunological reaction”

From the Journal Lupus • November 2009

Adjuvants and autoimmunity

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Abstract

Some adjuvants may exert adverse effects upon injection or, on the other hand, may not trigger a full immunological reaction. The mechanisms underlying adjuvant adverse effects are under renewed scrutiny because of the enormous implications for vaccine development. In the search for new and safer adjuvants, several new adjuvants were developed by pharmaceutical companies utilizing new immunological and chemical innovations. The ability of the immune system to recognize molecules that are broadly shared by pathogens is, in part, due to the presence of special immune receptors called toll-like receptors (TLRs) that are expressed on leukocyte membranes. The very fact that TLR activation leads to adaptive immune responses to foreign entities explains why so many adjuvants used today in vaccinations are developed to mimic TLR ligands. Alongside their supportive role, adjuvants were found to inflict by themselves an illness of autoimmune nature, defined as ‘the adjuvant diseases’. The debatable question of silicone as an adjuvant and connective tissue diseases, as well as the Gulf War syndrome and macrophagic myofaciitis which followed multiple injections of aluminium-based vaccines, are presented here. Owing to the adverse effects exerted by adjuvants, there is no doubt that safer adjuvants need to be developed and incorporated into future vaccines. Other needs in light of new vaccine technologies are adjuvants suitable for use with mucosally delivered vaccines, DNA vaccines, cancer and autoimmunity vaccines. In particular, there is demand for safe and non-toxic adjuvants able to stimulate cellular (Th1) immunity. More adjuvants were approved to date besides alum for human vaccines, including MF59 in some viral vaccines, MPL, AS04, AS01B and AS02A against viral and parasitic infections, virosomes for HBV, HPV and HAV, and cholera toxin for cholera. Perhaps future adjuvants occupying other putative receptors will be employed to bypass the TLR signaling pathway completely in order to circumvent common side effects of adjuvant-activated TLRs such as local inflammation and the general malaise felt because of the costly whole-body immune

http://www.ncbi.nlm.nih.gov/pubmed/19880572

From the Journal Medical Hypotheses • April 2002

Gulf war syndrome: could it be triggered by biological warfare-vaccines using pertussis as an adjuvant?

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Abstract

Several recent epidemiological studies have shown that vaccinations against biological warfare using pertussis as an adjuvant were associated with the Gulf war syndrome. If such epidemiological findings are confirmed, we propose that the use of pertussis as an adjuvant could trigger neurodegeneration through induction of interleukin-1beta secretion in the brain. In turn, neuronal lesions may be sustained by stress or neurotoxic chemical combinations. Particular susceptibility for IL-1beta secretion and potential distant neuronal damage could provide an explanation for the diversity of the symptoms observed on veterans.

http://www.ncbi.nlm.nih.gov/pubmed/12027522

“Several recent epidemiological studies have shown that vaccinations against biological warfare using pertussis as an adjuvant were associated with the Gulf war syndrome”

From the Journal Adverse Drug Reactions and Toxicological Review
March 1998

GWS

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Abstract

Since the end of the Gulf War, tens of thousands of American, Canadian and British soldiers who participated in that war have claimed to be suffering from a variety of incapacitating symptoms which are generally termed as Gulf War Syndrome (GWS). The symptoms are multiple but mainly consist of excessive tiredness, muscle and joint pain, loss of balance, sensory symptoms, neurobehavioural manifestations, diarrhoea, bladder dysfunction, sweating disturbances, and respiratory, gastrointestinal, musculoskeletal and skin manifestations. These veterans have been exposed to a variety of damaging or potentially damaging risk factors including environmental adversities, pesticides such as organophosphate chemicals, skin insect repellents, medical agents such as pyridostigmine bromide (NAPS), possible low-levels of chemical warfare agents, multiple vaccinations in combinations, depleted uranium, and other factors. A large number of basic research findings, clinical epidemiological studies, and case control studies are reviewed to try and link them together to produce a coherent picture and to demonstrate the complexity of the interaction of biological systems, environmental and genetic factors, combinations of drugs and toxins with human health. The findings of these studies so far have demonstrated that many of the previous assumptions made about the 'safety' of certain drugs and toxic substances or vaccines must be radically reviewed. Many of the findings have far reaching implications not only in terms of explanation of what might have gone wrong during the Gulf War, but also have wider implications for many occupational groups who are exposed daily to some of these risk factors. More open-mindedness and much less prejudice are required concerning the basic biology of interactions of the above factors and their effects on cell functions and wider intelligent research is urgently required with high priority. This review highlights the importance of intelligent research for answers for a new phenomenon, and demonstrates the necessity for a combination of this approach with high quality epidemiological research. The reader will notice an emerging clear picture that the majority (if not all) of these advances have been achieved from studies funded by independent or charity organizations rather than by the responsible authorities who are supposed and are duty bound to take on this task.

http://www.ncbi.nlm.nih.gov/pubmed/9638279

Gulf War syndrome: a model for the complexity of biological and environmental interaction with human health

Q&A: what is ASIA?

An interview with Yehuda Shoenfeld

In this Q&A, we talk to Professor Yehuda Shoenfeld about Autoimmune Syndrome Induced by Adjuvants (ASIA) and discuss his recommendations regarding further research in the field.

Professor Yehuda Shoenfeld is the founder and head of the Zabludowicz Center for Autoimmune Diseases at the Sheba Medical Center, which is affiliated to the Sackler Faculty of Medicine at Tel-Aviv University, Israel. He is also the Incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases at Tel-Aviv University. His clinical and scientific works focus on autoimmune and rheumatic diseases, and he has been the recipient of multiple awards, including a Life Contribution Prize in Internal Medicine in Israel, 2012.

In recent years, Professor Shoenfeld noted that four conditions: siliconosis, Gulf War syndrome (GWS), macrophagicmyofasciitis syndrome (MMF) and post-vaccination phenomena were linked with previous exposure to an adjuvant, and that the patients also presented with similar clinical symptoms. In 2011, this led Professor Shoenfeld to suggest these comparable conditions should be grouped under a common syndrome entitled 'ASIA', for 'Autoimmune (Autoinflammatory) Syndrome Induced by Adjuvants'.

What is ASIA?

ASIA is a new syndrome, which refers to autoimmune syndromes induced by adjuvants. It includes several conditions that are not fully characterized as autoimmune diseases like systemic lupus, rheumatoid arthritis or scleroderma, but that are induced by chronic stimulation of the immune system by substances which may react as adjuvants. This chronic stimulation leads to the emergence of these new signs and symptoms, which include fatigue, arthritis, myalgia, and neurological manifestations.

Which adjuvants commonly used in medical practice have been implicated in ASIA?

The idea of ASIA as a new syndrome developed after some studies on Gulf War syndrome reported that soldiers who had not been deployed to the Gulf area were suffering from symptoms such as severe fatigue, cognitive impairment, myalgias and arthralgias. This raised the question of whether it was the vaccines administered to the soldiers that induced these syndromes. The most common adjuvants are silicone implants and aluminum in vaccines.

Are any other adjuvants associated with ASIA?

There are some specific adjuvants which have been shown to induce ASIA; for instance, aluminium. Aluminium is the oldest, the cheapest and the most efficient adjuvant so far, which is why it is still commonly used in the development of vaccines.
In 2001, Romain Gherardi and colleagues reported that patients diagnosed with macrophagic myofasciitis, or MMF (a rare muscle disease characterized by specific myopathological alterations, first described by the Groupe d'Etudes et Recherche sur les Maladies Musculaires Acquises et Dysimmunitaires (GERMMAD)), had previously been vaccinated with hepatitis vaccines containing aluminium hydroxide. These patients went on to develop severe myalgia with neurological manifestations, cognitive impairment, dizziness, inability to concentrate and poor sleep. Following many studies, Romain Gherardi and colleagues were able to demonstrate that the aluminium is deposited in the muscle, and then via macrophages travels from the muscles to different organs and penetrates the blood-brain barrier. On this basis, MMF is part of the ASIA syndrome.

Another condition termed the 'sick building syndrome' (SBS) leads to similar clinical symptoms as the Gulf War syndrome, and manifests in people living in a specific room or building. However, once they move to another room or to another building, they completely recover. It is believed that, in that room, there is some substance that reacts or behaves like the adjuvant. I have already mentioned that aluminium is used as an adjuvant in vaccines, but as one of the most common materials in the world its uses are even more widespread, as much of the equipment we use in our daily lives is made from aluminium.

As the use of vaccines, silicone implants, etc., is widespread, what does this mean in terms of public health?

First of all, vaccines are very widespread, and I would like to clarify that I am definitely not against vaccines! Vaccines are the best medical development that humankind has had in the last 300 years, and have helped to bring about almost complete eradication of some viral diseases. However, it should be considered that when you give millions of people an active substance, and vaccines are active substances, then some may suffer from adverse events. After all, vaccines contain viral or synthetic particles emulsified in adjuvant, which is supposed to enhance the immune reaction.

So, we have to identify the people who are at risk of suffering from side effects due to the chronic stimulation of their immune system. First of all we have to diagnose them, to treat them—and some of them should be compensated, because the vaccines are quite often imposed on them either by the state, the government, or by the employer.

With regard to silicone implants, which is a very common cosmetic operation, there have been claims that the silicone is completely inert, that it doesn't leak and travel through the body, that it doesn't induce granulomas, etc., but this is misleading. There have been recent cases of ruptured silicone implants, but even with unruptured implants, there are nanoparticles of silicone that can travel through the body. Therefore silicone can be found in different parts, such as the hands, the chest and the groin. Although silicone implants are quite common, luckily enough the syndrome itself is rare.

Similarly, autoimmune diseases which are definitely induced by infections are not as common as the infections themselves. This is because a specific interaction between the infective agent and the genetic components is linked to incidence of autoimmune diseases.

With regard to the ASIA syndrome, prevalence is

higher in subjects that carry the gene HLA-DRB1. It should be noted that this is the same HLA (human leukocyte antigen) which was found to be present in those who had developed an autoimmune disease following vaccine administration. So, maybe in the future with further advances in personalized medicine, we will be able to screen those at risk based on their genetic composition, and therefore avoid onset of autoimmune diseases by avoiding administration of vaccines containing adjuvants that are known to be associated with the ASIA syndrome. In test subjects the type of adjuvant can be replaced with one that might not be associated with the ASIA syndrome. I would like to emphasize that currently there are novel adjuvants in development which have to be tested for efficacy, but we hope these might have fewer side effects than aluminium and other established adjuvants.

What are the current criteria used for diagnosis of ASIA?

We have published the criteria and classified it as we do usually with different autoimmune diseases, namely into major criteria and minor criteria. Major criteria include clinical manifestations such as severe fatigue, poor sleep, myalgia and arthralgia; the minor criteria include the presence of various autoantibodies and specific HLA (e.g., DRB1). However, as I mentioned before, over the years many of these patients may go on to develop a more well-defined autoimmune disease. For instance, if they develop scleroderma or systemic sclerosis, they will suffer from tight skin, complications of the lungs, kidneys, and so forth.

Have the mechanisms via which adjuvants may cause these effects been established?

In part, the mechanism involves the chronic stimulation of the immune system, which may then lead to the release of inflammatory cytokines including interferon, interleukin (IL)-1, IL-6, tumor necrosis factor (TNF) and so forth. So in part, this syndrome can be induced by this cascade of cytokines released in response to the chronic stimulation.

This chronic stimulation may also involve the opening of the blood-brain barrier, and therefore penetration of different substances into the brain. For example, one of the mechanisms which has been well defined is that aluminium deposits in the body following vaccine injection, or following exposure to other sources of aluminium, and these particles can cross the blood-brain barrier via macrophages and deposit in the brain.

In the past, we physicians witnessed this aluminium 'toxicity' of the brain in cases where the patient went through dialysis. The dialysate fluid contained aluminium, and actually diffused into the brain through the blood-brain barrier leading to aluminium intoxication. In some cases, the patient presented with symptoms consistent with the ASIA syndrome.

In addition, chronic stimulation also induces different autoantibodies. Although the autoantibodies do not necessarily indicate a specific autoimmune disease, it might be a combination of anti-DNA antibody which is more classic for systemic lupus erythematosus (SLE), but also anti-mitochondrial antibodies which may indicate primary biliary cirrhosis. As I mentioned earlier, the undefined connective tissue diseases (UCTD) over the years may develop to a specific autoimmune disease. Therefore we also believe that most cases of UCTD are actually part of ASIA syndrome.

Is there any evidence to suggest that environmental or genetic factors may lead to higher risk of developing ASIA?

The actual prevalence of environmental factors, in addition to silicone implants and the adjuvants in the vaccine, is not yet known. But based on my experience and from reading the literature, I can assume that aluminium and other different materials used in daily life may be associated. For instance, in the 1980s a significant increase in lupus cases was observed in an ex-industrial town in the United States: East Ferry Street in Buffalo, New York. Following investigations it was found that the area was heavily contaminated with toxic materials (including lead, polychlorinated biphenyls, trichloroethylene and volatile organic compounds).

So, looking at this from a wider context I would say that it can be considered that toxic materials which can act like the adjuvants may underlie what we call 'idiopathic' autoimmune diseases.

What is known about the prevalence of ASIA, particularly in terms of geographical distribution?

There is no knowledge about geographical distribution. We do know that many of the autoimmune diseases are more prevalent in populations that live further away from the equator. It is believed that limited exposure to sun, and therefore the lack of production of vitamin D, may be associated with ASIA. We know that vitamin D is associated with many autoimmune diseases. For instance, in one study we analyzed more than 40 different autoimmune diseases, and found the patients had significantly lower levels of vitamin D in comparison with the healthy population within the same geographical area.

Studies have emerged from the Philippines, Mexico, from all over the world, but these are just small series of cases. There are no large epidemiological studies so far that have been able to analyze the geographical distribution. However, I believe that eventually we will find a correlation between the ASIA syndrome and geographical distribution.

One study from Finland reported a large increase in cases of narcolepsy, which is now recognized as an autoimmune condition. The researchers correlated this increase of narcolepsy incidences with the vaccines which were administered during the H1N1 (swine flu) epidemic in that region.

I would like to emphasize that this disease is recognized in Finland and is strictly associated with the (HLA) DQB1*0602 genotype. When the vaccine was delivered during the H1N1 epidemic, there was a 13-fold increase of narcolepsy in this geographical area. So the geographic distribution in this case was not connected to the substance, but rather to the genotype of the people who live in the area, which made them more susceptible to developing narcolepsy.

What do you think are the future directions of research into this field?

Efforts should be made to understand the mechanisms behind ASIA and to develop better adjuvants, especially in vaccines. After all, numerous people are vaccinated regularly, and we should minimize any potential side effects.

We should learn from ASIA to better understand the etiology of other autoimmune diseases that are currently regarded as 'idiopathic' (which means that we are idiots as we don't know the pathology and etiology!). I would like that in the future, I will not see the sentence 'autoimmune diseases have an unknown etiology', because we are coming closer to better understanding this.

I am still concerned about silicone implants; whether to recommend these should be explanted or not, as there is no guarantee of full recovery from the ASIA syndrome if the silicone implants are explanted. If not, then the patient is left without the implants and continue to suffer from the ASIA syndrome. Having said that however, there are a few cases where explanting led to a complete recovery of the patient from the ASIA syndrome. This requires further investigation.

A lot of research is going on all over the world, and I hope that in the future we'll be able to better identify those who are at risk of developing this syndrome, and to avoid it before they do.

What is your advice to clinicians for the management and treatment of patients with autoimmune disorders? Should they be routinely screened for ASIA?

As there are no markers for ASIA, we cannot screen for this. My advice to the clinician is to pay more attention to the history of the patient, specifically regarding their vaccine history. In the future, I would like for clinicians to be able to diagnose the patient early on, and in addition may help to compensate them if appropriate; after all, these patients suffer. They were completely healthy until they were vaccinated and then suddenly developed the disease.

Better understanding of the symptoms and development of serological markers may help to identify the risk factors such as HLA and familial autoimmune background at a very early stage. The therapy for ASIA should be the same therapy as for autoimmune diseases—and until we can understand it better, maybe clinicians should consider switching to other biological drugs that have not been associated with ASIA, rather than continue to use the drugs that have been.

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“Findings suggest that U.S. male neonates vaccinated with the hepatitis B vaccine prior to 1999 (from vaccination record) had a threefold higher risk for parental report of autism diagnosis compared to boys not vaccinated as neonates during that same time period”

Hepatitis B vaccination of male neonates and autism diagnosis,
NHIS 1997-2002, Journal of Toxicology and Environmental Health, 2010:

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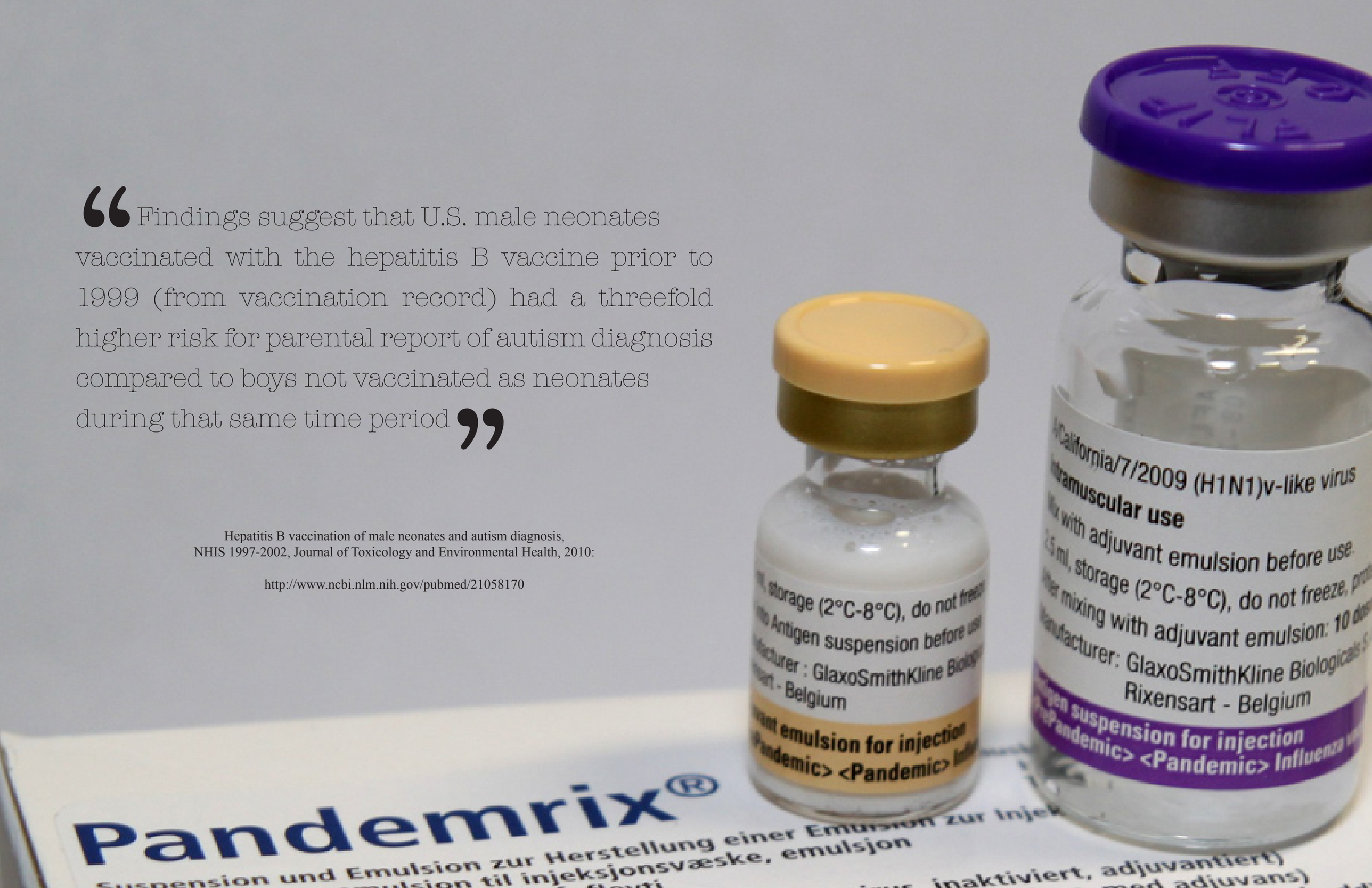
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From the Journal Cellular Immunology
Volume 73, Issue 2, 1 November 1982, Pages 299–310

Acute experimental autoimmune encephalomyelitis in mice: Adjuvant action of Bordetella pertussis is due to vasoactive amine sensitization and increased vascular permeability of the central nervous system

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Abstract

Experimental autoimmune encephalomyelitis (EAE) in mice is dependent upon the use of Bordetella pertussis suspensions as an adjuvant. Intravenous administration of B. pertussis causes an increased vascular permeability in brain tissue and an increased vascular sensitivity to vasoactive amines which promotes the development of EAE. The efficacy of different batches and strains of B. pertussis in the expression of EAE closely correlates with the vasoactive amine sensitization activity of each material tested. Pertussigen, the histamine sensitizing factor (HSF), is responsible for these adjuvant properties whereas purified endotoxin is inactive. The effect of cimetidine, diphenhydramine, methysergide, reserpine, and cyproheptadine on B. pertussis induced histamine sensitivity and the expression of EAE are examined. Cyproheptadine, an agent with mixed histamine and serotonin blocking properties, blocks both B. pertussis-induced vasoactive amine sensitization and the expression of EAE.

http://www.sciencedirect.com/science/article/pii/0008874982904579

“Intravenous administration of B. pertussis causes an increased vascular permeability in brain tissue and an increased vascular sensitivity to vasoactive amines which promotes the development of EAE”

From the Journal Immunology • July 2002

Pertussis toxin modulates the immune response to neuroantigens injected in incomplete Freund's adjuvant: induction of Th1 cells and experimental autoimmune encephalomyelitis in the presence of high frequencies of Th2 cells

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Abstract

Pertussis toxin (PT) has been widely used to facilitate the induction of experimental autoimmune encephalomyelitis (EAE) in rodents. It has been suggested that this microbial product promotes EAE by opening up the blood-brain barrier and thereby facilitates the migration of pathogenic T cells to the CNS. However, PT has other biological effects that could contribute to its activity in EAE, such as enhancing the cytokine production by T cells and induction of lymphocytosis. In this work, we investigated the effects of PT on the pathogenicity, cytokine differentiation, and clonal sizes of neuroantigen-reactive T cells in EAE in mice. Our results show that PT prevented the protection from EAE conferred by injection of PLPp139-151 in IFA and induced high frequencies of peptide-specific Th1 cells and disease. Interestingly, the mice developed EAE despite the simultaneous vigorous clonal expansion of PLPp139-151-specific Th2 cells. The data indicate that the Th2 cells in this model neither were protective against EAE nor promoted the disease. Furthermore, the results suggested that the effects of the toxin on neuroantigen-reactive T cells were promoted by the PT-induced activation of APCs in lymphoid tissues and the CNS. Together, the results suggest that microbial products, such as PT, could contribute to the initiation of autoimmune disease by modulating the interaction between the innate and adaptive immune system in the response to self Ags.

http://www.jimmunol.org/content/169/1/117.long

> "the results suggest that microbial products, such as PT [Pertussis Toxin], could contribute to the initiation of autoimmune disease"

Immunization Safety Review: SV40 Contamination of Polio Vaccine and Cancer

Institute of Medicine (US) Immunization Safety Review Committee;
Stratton K, Almario DA, McCormick MC, editors.

Washington (DC): National Academies Press (US); 2002

Excerpt

Some of the polio vaccine administered from 1955–1963 was contaminated with a virus, called simian virus 40 (SV40). The virus came from the monkey kidney cell cultures used to produce the vaccine. Most, but not all, of the contamination was in the inactivated polio vaccine (IPV). Once the contamination was recognized, steps were taken to eliminate it from future vaccines. Researchers have long wondered about the effects of the contaminated vaccine on people who received it. Although SV40 has biological properties consistent with a cancer-causing virus, it has not been conclusively established whether it might have caused cancer in humans. Studies of groups of people who received polio vaccine during 1955–1963 provide evidence of no increased cancer risk. However, because these epidemiologic studies are sufficiently flawed, the Institute of Medicine's Immunization Safety Review Committee concluded that the evidence was inadequate to conclude whether or not the contaminated polio vaccine caused cancer. In light of the biological evidence supporting the theory that SV40-contamination of polio vaccines could contribute to human cancers, the committee recommends continued public health attention in the form of policy analysis, communication, and targeted biological research.

http://www.ncbi.nlm.nih.gov/pubmed/25057632

Increased risk of non-influenza respiratory virus infections associated with receipt of inactivated influenza vaccine

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Our experimental study provides evidence consistent with temporary non-specific immunity against other respiratory viruses following influenza virus infection, a phenomenon that could explain the epidemiologic dynamics of respiratory virus epidemics described in ecologic studies.

Abstract

We randomized 115 children to trivalent inactivated influenza vaccine (TIV) or placebo. Over the following 9 months, TIV recipients had increased risk of virologically-confirmed non-influenza infections (relative risk: 4.40; 95% confidence interval: 1.31-14.8). Being protected against influenza, TIV recipients may lack temporary non-specific immunity that protected against other respiratory viruses.

http://cid.oxfordjournals.org/content/early/2012/03/13/cid.cis307

> “TIV recipients had increased risk of virologically-confirmed non-influenza infections”

Impact of Repeated Vaccination on Vaccine Effectiveness Against Influenza A(H3N2) and B During 8 Seasons

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Abstract

Background: Recent studies suggest that influenza vaccination in the previous season may influence the effectiveness of current-season vaccination, but this has not been assessed in a single population over multiple years.

Methods. Patients presenting with acute respiratory illness were prospectively enrolled during the 2004–2005 through 2012–2013 influenza seasons. Respiratory swabs were tested for influenza and vaccination dates obtained from a validated registry. Vaccination status was determined for the current, previous, and prior 5 seasons. Vaccine effectiveness (VE) was calculated for participants aged ≥9 years using logistic regression models with an interaction term for vaccination history.

Results: There were 7315 enrollments during 8 seasons; 1056 (14%) and 650 (9%) were positive for influenza A(H3N2) and B, respectively. Vaccination during current only, previous only, or both seasons yielded similar protection against H3N2 (adjusted VE range, 31%–36%) and B (52%–66%). In the analysis using 5 years of historical vaccination data, current season VE against H3N2 was significantly higher among vaccinated individuals with no prior vaccination history (65%; 95% confidence interval [CI], 36%–80%) compared with vaccinated individuals with a frequent vaccination history (24%; 95% CI, 3%–41%; P = .01). VE against B was 75% (95% CI, 50%–87%) and 48% (95% CI, 29%–62%), respectively (P = .05). Similar findings were observed when analysis was restricted to adults 18–49 years.

Conclusion: Current and previous-season vaccination generated similar levels of protection, and vaccine-induced protection was greatest for individuals not vaccinated during the prior 5 years. Additional studies are needed to understand the long-term effects of annual vaccination.

http://cid.oxfordjournals.org/content/early/2014/09/29/cid.ciu680.full

From the Journal Clinical Infectious Diseases • May 2013

Influenza vaccine effectiveness in the community and the household

Ohmit SE, Petrie JG, Malosh RE, Cowling BJ, Thompson MG, Shay DK, Monto AS.

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Abstract

BACKGROUND:

There is a recognized need to determine influenza vaccine effectiveness on an annual basis and a long history of studying respiratory illnesses in households.

METHODS:

We recruited 328 households with 1441 members, including 839 children, and followed them during the 2010-2011 influenza season. Specimens were collected from subjects with reported acute respiratory illnesses and tested by real-time reverse transcriptase polymerase chain reaction. Receipt of influenza vaccine was defined based on documented evidence of vaccination in medical records or an immunization registry. The effectiveness of 2010-2011 influenza vaccination in preventing laboratory-confirmed influenza was estimated using Cox proportional hazards models adjusted for age and presence of high-risk condition, and stratified by prior season (2009-2010) vaccination status.

RESULTS:

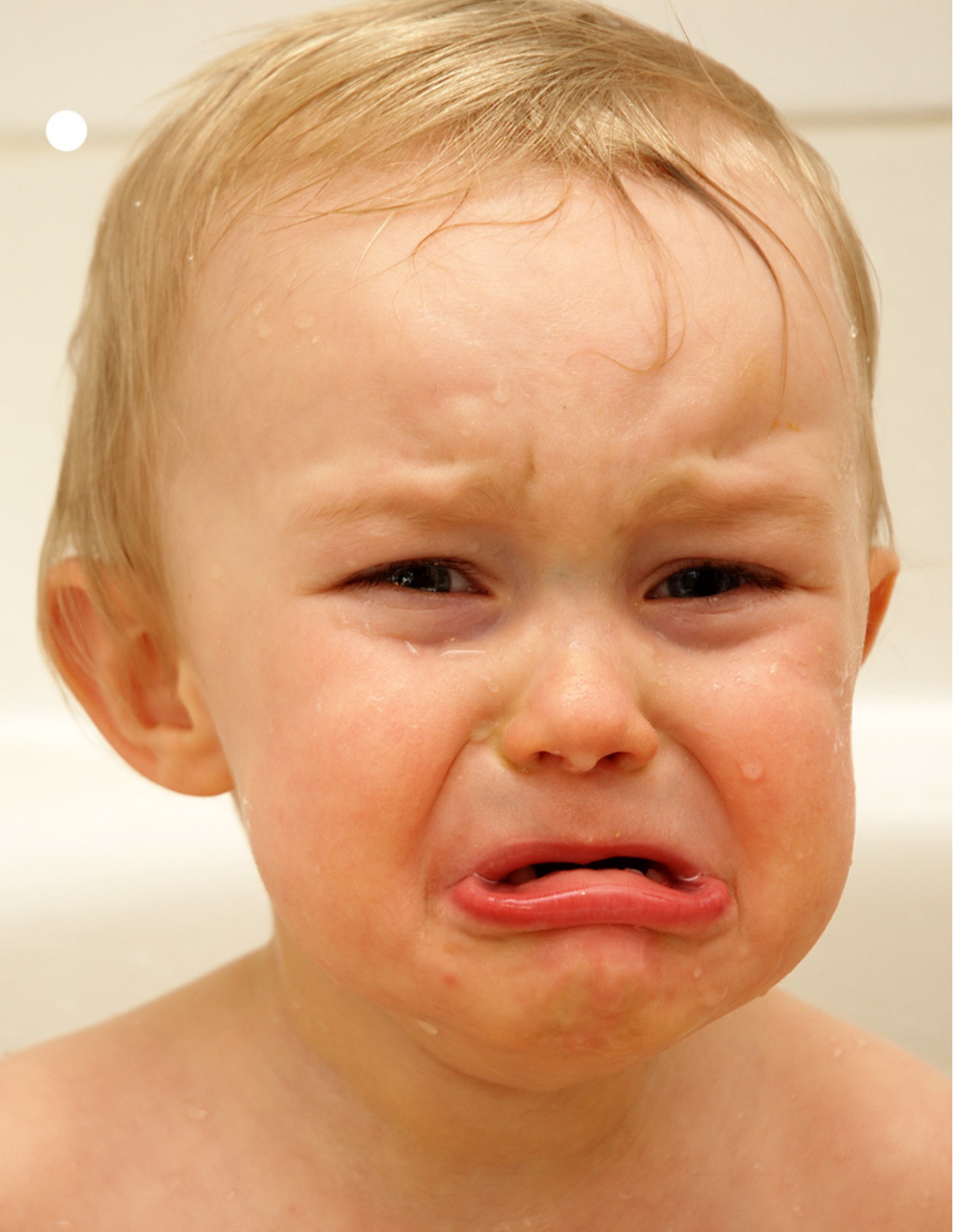
Influenza was identified in 78 (24%) households and 125 (9%) individuals; the infection risk was 8.5% in the vaccinated and 8.9% in the unvaccinated (P = .83). Adjusted vaccine effectiveness in preventing community-acquired influenza was 31% (95% confidence interval [CI], -7% to 55%). In vaccinated subjects with no evidence of prior season vaccination, significant protection (62% [95% CI, 17%-82%]) against community-acquired influenza was demonstrated. Substantially lower effectiveness was noted among subjects who were vaccinated in both the current and prior season. There was no evidence that vaccination prevented household transmission once influenza was introduced; adults were at particular risk despite vaccination.

CONCLUSIONS:

Vaccine effectiveness estimates were lower than those demonstrated in other observational studies carried out during the same season. The unexpected findings of lower effectiveness with repeated vaccination and no protection given household exposure require further study.

http://www.ncbi.nlm.nih.gov/pubmed/23413420

> “The unexpected findings of lower effectiveness with repeated vaccination and no protection ... require further study”



Neurodevelopmental Disorders after Thimerosal-Containing Vaccines: A Brief Communication

Mark R. Geier and David A. Geier

Experimental Biology And Medicine • 2003
The Genetic Centers of America, Silver Spring, Maryland 20905

Abstract

We were initially highly skeptical that differences in the concen- trations of thimerosal in vaccines would have any effect on the incidence rate of neurodevelopmental disorders after childhood immunization. This study presents the first epidemiologic evi- dence, based upon tens of millions of doses of vaccine admin- istered in the United States, that associates increasing thimero- sal from vaccines with neurodevelopmental disorders. Specifi- cally, an analysis of the Vaccine Adverse Events Reporting System (VAERS) database showed statistical increases in the incidence rate of autism (relative risk [RR] = 6.0), mental retar- dation (RR = 6.1), and speech disorders (RR = 2.2) after thimero- sal-containing diphtheria, tetanus, and acellular pertussis (DTaP) vaccines in comparison with thimerosal-free DTaP vac- cines. The male/female ratio indicated that autism (17) and speech disorders (2.3) were reported more in males than fe- males after thimerosal-containing DTaP vaccines, whereas mental retardation (1.2) was more evenly reported among male and female vaccine recipients. Controls were employed to de- termine if biases were present in the data, but none were found. It was determined that overall adverse reactions were reported in similar-aged populations after thimerosal-containing DTaP (2.4 ± 3.2 years old) and thimerosal-free DTaP (2.1 ± 2.8 years old) vaccinations. Acute control adverse reactions such as deaths (RR = 1.0), vasculitis (RR = 1.2), seizures (RR = 1.6), ED visits (RR = 1.4), total adverse reactions (RR = 1.4), and gastro- enteritis (RR = 1.1) were reported similarly after thimerosal- containing and thimerosal-free DTaP vaccines. An association be- tween neurodevelopmental disorders and thimerosal- containing DTaP vaccines was found, but additional studies should be conducted to confirm and extend this study.

http://mercury-freedrugs.org/docs/NeurodevelopmentalDisordersAfterThimerosal-ContainingVaccines-A%20Brief%20Communication.pdf

> “An association between neurodevelopmental disorders and thimerosal containing DTaP vaccines was found”

The End